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BROWN-SÉQUARD SYNDROME

A Case of Unusual Ætiology

BY

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THAT hypernephromata frequently give rise to metastases in the central nervous system and its coverings is well known. The location of the secondary growths is most frequent in the bones of the skull and vertebral column and in the substance of the brain. Extension from the vertebral column or from the spinal meninges may ultimately give rise to symptoms of pressure on the spinal cord, but a case where the first and last symptoms of the tumour were due to invasion of the medulla spinalis and where at autopsy this was found to be the only lesion outside the primary tumour is sufficiently rare to warrant its being put on record.

Since Augstein (1921) has reviewed the subject there is little point in discussing the general question of the site of hypernephromatous secondaries. The literature abounds in accounts of metastases in bone, lung, liver, adrenal, and other tissues, but there are, so far as can be determined from a search of the literature, only two cases of spinal intramedullary metastasis. A case reported by Belz (1912) showed a mass in the lumbar cord extending into the upper sacral region. The author shows without doubt the intramedullary nature of the secondary, there being no involvement of the spinal coverings. Other features of the case were secondaries in the liver and a recurrent growth with involvement of the associated lymph nodes at the site of the original tumour six months after the removal of the primary mass. The appearance of the metastasis in the spinal cord is very similar to that in the present case. V. Pfungen (1906) reported a case of metastatic growth from a hypernephroma where the secondary was completely intramedullary and was situated at the level of the second cervical segment; hæmorrhage had occurred into the

secondary and had given rise to a hæmatomyelia. No histological picture of the secondary is given. The primary growth had been removed one year before the onset of neurological symptoms.

Personal Case

W. S., a male 62 years of age, was admitted to the Western Infirmary of Glasgow on 29th October, 1936. His complaint was loss of power in the right leg of seven weeks' duration. He gave the following history. Seven weeks before admission he felt tingling and numbness in the toes of the right foot. Gradually these symptoms spread to involve the whole extremity. This extension was accompanied by a progressive loss of power in the affected leg. He felt that the leg had become useless and he volunteered the information that he had no knowledge of the posture of the limb. At the same time he became aware that stimuli which normally caused pain no longer did so when applied to the left leg. For some weeks before admission he had precipitancy of micturition, which, within the past week, had given place to incontinence of urine. On admission there was some pain in the region of the right scapular angle, which pain occasionally radiated to the front of the body.

Until seven weeks before admission to hospital his health was excellent and apart from the diseases of childhood he had never been ill. No facts of any present significance were recorded in the family history.

Clinical Examination.—October 30, 1936. The patient is very obese. He is uncomfortable as he lies in bed. The face is pale and slightly cyanotic. There is no complaint of pain, but some sense of discomfort is experienced in the right leg. The right leg lies immobile save for some involuntary twitching. Wasting is not in evidence. The nutrition of the skin over the sacrum is seriously impaired, but the surface is not actually broken.

Circulatory System.—The pulse rate was 94 per minute. The beats were regular in volume and in rhythm. The apex beat was impalpable. The transverse dimension of the area of cardiac dulness measured 4 in. to the left of the right border, which was situated ¼ in. to the right of the middle line. The systolic blood pressure was 160 mm. Hg., while the diastolic was 90.

Respiratory System.—No abnormality was detected.

Alimentary System.—The tongue was slightly furred. The abdominal wall was very obese ; palpation revealed no local or general tenderness nor was any mass felt in the abdomen.

Urinary System.—The urine contained no pathological constituents.

Nervous System (see Diagram 1).—Examination revealed no abnormality in function of any of the cranial nerves. Sensory and motor functions and the deep reflexes in the upper extremities and shoulder girdle were normal. The abdominal and cremasteric reflexes were absent on both sides. The right patellar and Achilles' tendon reflexes were much more hyperactive than the brisk reflexes of the opposite limb. The plantar response was extensor in type on both sides. The right leg could not be moved voluntarily. Increased resistance to passive movement was not a marked feature, but clonus was elicited at the right knee and ankle. Sensory tests revealed a complete anæsthesia to pin-prick in the skin of the left inferior extremity. This area of anæsthesia was continuous, with a similar defect extending up to and involving the eighth dorsal segment. There was impairment without absolute loss of pain sensibility in the skin of the sixth and seventh dorsal segments of the left side. The area over which impairment of temperature sensibility was observed was practically co-extensive with that just described. Touch was appreciated well on both sides. Postural sensibility was intact in the left lower limb, but was entirely absent in the right. Vibration sensibility as tested by tuning fork was absent over the bony prominences of both inferior extremities except over the left internal malleolus, where vibration was appreciated only to a very slight extent.

Lumbar Puncture.—This procedure showed a cerebrospinal fluid pressure of 150 mm. C.S.F. Compression of the jugular veins was attended by a rapid rise in pressure which fell quickly on release. Cells in the cerebrospinal fluid numbered 2 per c.mm. There was no increase in the protein content and the Wassermann reaction was negative. Shortly after the performance of the lumbar puncture the

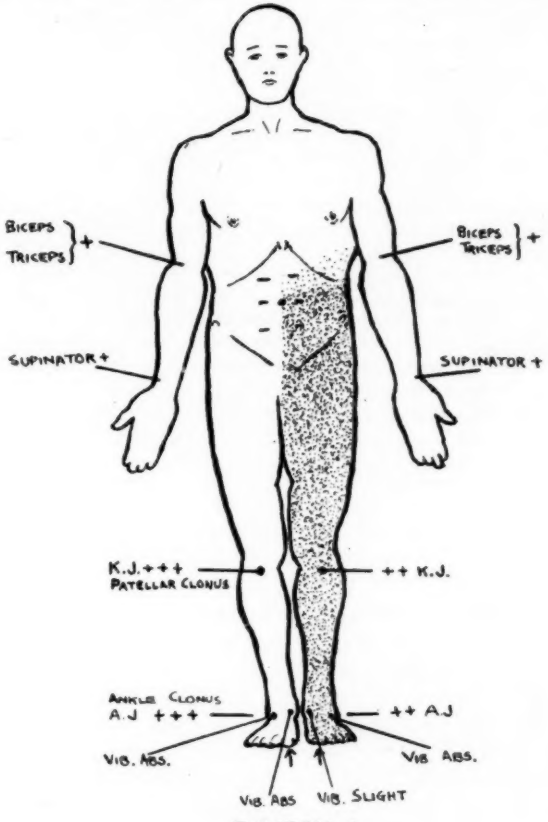

DIAGRAM 1.

SUMMARY OF THE PRINCIPAL FINDINGS. THE STIPPLED AREA REPRESENTS THE REGION OVER WHICH PAIN AND TEMPERATURE SENSIBILITY WERE LOST. PROPRIOCEPTIVE SENSIBILITY WAS LOST IN THE RIGHT LOWER LIMB BUT IS NOT INDICATED IN THE DIAGRAM.

patient died and went to autopsy with the clinical diagnosis of a right-sided lesion in the mid-dorsal region of the spinal cord ; the nature of the lesion was not suggested.

The following is a record of the more important findings of an autopsy carried out on 2nd November, 1936, 48 hours after death.

The body is that of a male subject with considerable excess of fat both in the subcutaneous tissue and other fat depots. The *peritoneal cavity* contains 60 c.c. of blood-stained fluid.

Both *kidneys* are enlarged (right 800 gm., left 280 gm.). The entire upper pole of the right kidney is occupied by a hypernephroma, 9 cm. by 8 cm. in its maximum longitudinal and transverse measurements. Hæmorrhage, necrosis, and autolysis are marked features of the growth. It has no capsule and has replaced the kidney substance of the upper pole, without, however, invading the renal vessels or pelvis. The surviving tissue and the whole of the left kidney show no important change. The lower urinary tract and both suprarenals are normal. The *spleen* is enlarged (300 gm.) and soft ; the *heart* is enlarged (480 gm.) and all its chambers are dilated. No secondary growths or other significant lesions are found in any of the thoracic or abdominal viscera.

Examination of the *central nervous system* shows only one lesion—a greyish-white, firm swelling in the right half of the spinal cord involving the eighth and ninth dorsal segments. This swelling produces only slight distortion of the normal shape of the spinal cord, since it is almost entirely intramedullary. The dura mater is not involved. The brain shows no flattening of the convolutions, but there is evidence of some degree of compression of the medulla, although without formation of an actual " pressure cone." The vertebral column, skull, and meninges show no abnormality.

The *spinal cord*, after fixation in formalin and examination, segment by segment, shows only the lesion in the eighth and ninth dorsal segments as described above. Sections prepared for microscopic examination after paraffin embedding of the tissue demonstrate that the *renal tumour* (Figs. 1 and 2) is a typical hypernephroma. In the parts least affected by degeneration and autolysis the delicate vascular stroma supporting numerous large vacuolated epithelial cells is readily made out. In certain parts of the growth the epithelial cells are arranged in acini, while in others they are grouped in more solid irregular masses with many aberrant types of cell. Figs. 3 and 4 clearly indicate that the tumour in the spinal cord is of identical structure.

The maximum involvement of the cord is at the ninth dorsal segment where the entire right half of the spinal medulla is replaced by tumour tissue. The tenth dorsal segment is not involved and the upper limit of the growth is found in the eighth dorsal segment. Tumour is present in the sheath and substance of the posterior nerve root entering the eighth dorsal segment.

The clinical interest in this case lies in the fact that a syndrome closely resembling that described by Brown-Séquard has arisen from an intraspinal metastasis. It is generally agreed that the pure syndrome is but rarely seen and that its usual ætiology is traumatic. The picture here is not quite classical, since there is an extensor plantar response on the left side and sensibility to vibratory stimuli was absent or much diminished over the bony points of the left inferior extremity. Two clinical anomalies are worthy of note. Sensibility to vibration was lost in the limb in which postural sense was well maintained. Thus apparently there is a contradiction of the classical view that the same pathway in the cord subserves conduction of the two forms of stimuli ; such a conclusion, however, implies equal vulnerability of the two systems. The other finding is that, in this case of cord neoplasm, the cerebrospinal fluid contained no excess of protein and cells.

We wish to express our thanks to Dr. John Gracie, in whose wards the patient was investigated, and to Mr. John Kirkpatrick of the Pathology Department for the photomicrographs.

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Fig. 1.—Tumour of kidney showing typical structure of hypernephroma. Mallory's connective tissue stain ; ×100.

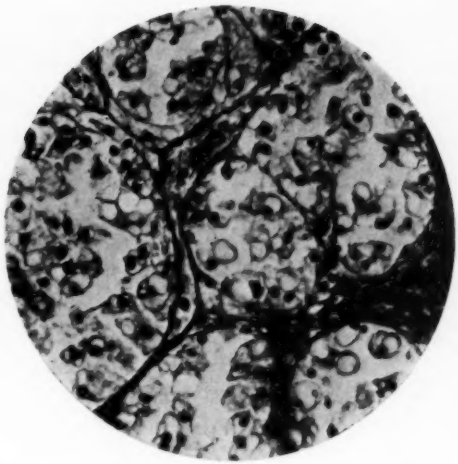

Fig. 2.—Higher magnification of Fig. 1 ; ×300.

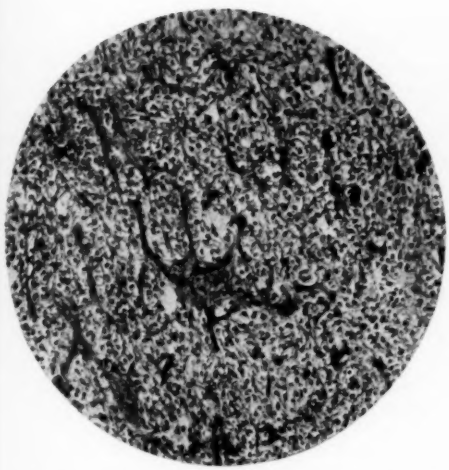

Fig. 3.—Tumour of spinal cord showing same general features as Fig. 1. Mallory's connective tissue stain ; ×100.

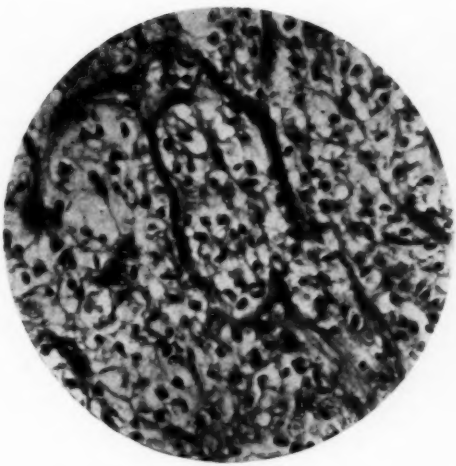

Fig. 4.—Higher magnification of Fig. 3 ; ×300.

RECENT STUDIES OF THE MORPHOLOGY OF THE NEURONE IN HEALTH AND DISEASE [1]

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Normal Neurone

THE modern conception of the structure of the neurone is founded mainly on the work of Cajal and of Nissl. Earlier observers, such as Waller, His, and Ranvier, had established the connection of the axone with the nerve cell and paved the way for the neurone theory, which was formulated almost in its present form by Cajal (1891) on the basis of purely morphological study. To his method of impregnation with reduced silver nitrate we owe our knowledge of the neurofibrillar structure of the neurone and of its reactions to injury or disease. Modern knowledge of the changes in the structure of the nerve cell in disease is, however, chiefly based on Nissl's studies by his polychrome methylene blue method. His classification stands to-day with minor modifications as the basis of neuronal pathology. The end of the life-work of Nissl and Cajal, therefore, forms a convenient starting-point for a survey of recent studies on the morphology of the neurone. It will be convenient first to examine the normal structure of the neurone as indicated by these researches, and secondly to review additions to knowledge of the changes which the neurone undergoes in disease.

THE PERIKARYON

Physical Constitution.—The examination of the fresh nerve cell with the ultra-microscope by Marinesco (1911) and Mott (1912) did not reveal any constituents which other methods had not shown. Rather, it made them cast doubts on the existence of Nissl granules and neurofibrils in a preformed state. It seemed to them that these structures could not be brought out without special staining technique and were to that extent artefacts. To-day, however, the existence of these structures in the living neurone may be considered as definitely established.

The physical constitution of living cells has been recently investigated by de Renyi (1931) and by Beams and King (1935). De Renyi studied the anterior horn cells of the frog, removed immediately after death, by the technique of micro-dissection. His researches on the nerve cell carried him no farther than to demonstrate the extremely high viscosity and toughness of the structure of

[1] The substance of this article formed the basis of the Oliver-Sharpey Lectures delivered before the Royal College of Physicians, London, in March, 1938.

the nerve cell. Thus if its opposite poles were transfixed and pulled away from one another, the cell tore across, leaving an irregular line of cleavage which remained unaltered for a short time, so that if the two halves were brought together again the anfractuosities of one-half fitted perfectly into those in the other, and the original outline of the cell was restored. Even the nucleus could be torn across and reconstituted in this manner. In addition, he was able to demonstrate the firm adhesion both of the dendrites of surrounding cells, and also, as he thought, of the neuroglial fibres, to the surface of the perikaryon, for it was very difficult to dislodge them with a jet of saline.

Beams and King have studied the physical properties of the nerve cell by the method of ultra-centrifugalization. Ingvar (1923) had studied the nerve cells of the mouse's brain by centrifugalization, but the length of time needed to cause more than minimal change at the speeds then available vitiated the results, as artefacts and post-mortem changes occurred. With the ultra-centrifuge more effect could be obtained after ten minutes than after an hour with the older instruments, and Beams and King considered that the changes which they found were influenced only to a slight degree by autolysis. In the cells of the spinal ganglion of the white rat they were unable to displace the nucleus from the centre of the cell, and therefore considered that it had the same density as the cytoplasm. The constituents of both nucleus and cell body could, however, be displaced. The nucleolus moved to the distal pole of the nucleus and became flattened against the nuclear membrane ; the other basophil structures in the nucleus (nuclein threads and granules) also became displaced to the periphery. The shape of the nucleus became altered by stretching in the direction of centrifugal force, so that it became cylindrical or shaped like an hour-glass. The contents of the nucleus lay in thin layers, most peripherally the nucleolus, next the chromatin filling about half the nucleus, and proximally a clear area of nuclear sap. In the perikaryon the Nissl granules were found to move in the direction of centrifugal force, usually retaining, at least during the earlier phases, their discrete character and ultimately becoming piled against the peripheral part of the cell membrane. The cytoplasm remaining in the proximal pole of the cell was slightly granular and strongly acidophilic.

" *Boutons terminaux*."—Fedorow (1935) has observed the living nerve cells in the superficial plexus of the frog's heart by the method of Gramenitzky (1934). Using a water-immersion lens bathed in Ringer's fluid he was able to study the cells in a state as nearly physiological as possible. He also observed their alterations under conditions of acidity and alkalinity, hypertonicity and hypotonicity of the fluid they were bathed in, with or without the addition of vital or supravital dyes. Under normal conditions it was possible to see small granules or drops attached to nerve fibres on the surface of the nerve cells and these were proved by vital staining with methylene blue to be " boutons terminaux." In the nerve cells nothing could be seen except the nucleus and pigment granules, the latter varying in number with the season of the year, being most numerous in winter. His most interesting observations bore on the effect of physico-chemical changes in the fluid which bathed the nerve cells or of the *p*H of the serum. He was able to correlate these effects with those

produced by mechanical injury or prolonged electrical stimulation. He observed two different types of early change in the " boutons terminaux," one which he termed " gelatinization," in which the discs became more sharply delimited and more intensely refractile, the other characterized by " swelling " of the discs, in which they became more rounded and transparent. " Gelatinization," which was reversible in its early stages, was produced by acidity, hypotonic solutions, and prolonged electrical stimulation of the vagus, and was also seen as a passing phase of degeneration following vagal section. It was usually associated with the appearance of granules in the cell body. The change described as " swelling," which always appeared to be irreversible, was produced by alkalis and hypertonic solutions.

The most important result of his work has been to establish the " boutons terminaux " as structures visible round the living nerve cell and showing during life the same appearances of degeneration (e.g. after section of the axone with which they are connected) as have been demonstrated in stained specimens. The degeneration of " boutons terminaux " affords a method of studying the terminations of nerve fibres and tracts, in relation to motor or sensory nuclei, which has recently been used with some success. Any observations, therefore, which give us more knowledge of their structure and of its variations under known conditions are of importance.

Pre-existence of the Neurofibrillar Network in Living Nerve Cells and Fibres. —The question of the existence of neurofibrils in the living nerve cell and fibre has excited much controversy. It has been known for some time that in certain lower forms, such as the jelly-fish, the crab, lobster, and torpedo, neurofibrils can be seen in fresh, unstained nerves. Kedrowski (1935) studied them in the antennæ of young living crustaceans (Branchipus, chirocephalus, apus), in which they appeared to be constantly moved about by the movement of the cytoplasm surrounding them. In these species the neurofibrils were seen in the bipolar nerve cells as well as in the nerve fibres arising from them. De Renyi (1929) saw them as a central core in the axis cylinders of the large nerves to the claw of the lobster, although he was unable to see them in frog's nerves ; and he argues from this that they are actually present in vertebrate nerves, but that owing to their finely filamentous structure, to their close juxtaposition in the axone, and to the comparatively slight difference in refractile power between them and axoplasma, they cannot be seen under the microscope. Weiss and Wang (1936) and Levi and Meyer (1937), independently, have seen them in tissue cultures from the nervous system of 11–14-day chicken embryos. Especially when the nerve cells in spreading out from the explant became isolated and somewhat flattened was it possible to see a definite fibrillar structure in the cell body consisting of fine concentric lines converging on the axis cylinder hillock and traceable into the proximal part of the axon. In the more peripheral part of the axone in which neurofibrils are presumably more closely set, they were not visible, nor were they seen in younger embryos and in earlier stages of tissue culture. Their appearance agreed with that seen after staining by Cajal's method, but varied in the same cell from day to day. In " younger " (Weiss and Wang) or " smaller " cells (Levi and Meyer) they lay in the peri-

nuclear zone of cytoplasm, leaving a clear zone between them and the cell membrane, and it was found that the mitochondria (or Janus green granules) lay altogether in this clear zone.

Levi and Meyer also studied the degenerative changes which the neurofibrils showed in cells in old cultures. In such cells the fine fibres ran together into coarser lines resembling those seen by Tello (1904) in hibernating lizards, and in mammals exposed to cold (Cajal, 1904 ; Donaggio, 1906). In more severely degenerating cells the neurofibrils were collected together in a clump of densely compressed fibres prolonged into the axis cylinder and were easily seen against the background of clear cytoplasm. These appearances closely resembled those seen in degenerated spinal root ganglion cells under a variety of conditions. The evidence which these experiments give as to the existence of neurofibrils in normal living vertebrate nerve cells may not be completely convincing, but they agree completely with de Renyi's theory that our inability to see neurofibrils in living axones is due rather to the imperfections of microscopical definition than to absence of preformed fibrillar structure in the nerve cell and fibre.

By photography with ultra-violet light Weimann (1925) was able to demonstrate in fresh nerve cells and their processes a network of fine threads which ran through, as well as between, the Nissl granules. There was no suggestion that the threads were made up of rows of rods and granules. Thenon and Pirowski (1937), using the same method, could not demonstrate any structure resembling neuro-fibrils. Both they and Weimann obtained beautiful pictures of Nissl granules in fresh nerve cells.

Mineral Composition.—The method of microincineration has been used during recent years to demonstrate the mineral composition of different tissues. It was applied to nerve cells by Jacobi and Keuscher (1927), and by many since them. All are agreed that the appearances seen in ashed sections by oblique or dark-ground illumination agree remarkably with those obtained by Nissl's method. Mineral deposits are only seen in the nucleolus and Nissl granules ; most of the nucleus, the neurofibrils, and the axone hillock appearing quite clear. The appearances seen by this method agree remarkably with those obtained by photographing nerve cells with ultra-violet light, and it has indeed been suggested that the opacity of different structures in a cell to ultra-violet light is related to their mineral content. The minerals in both nucleolus and Nissl granules are chiefly calcium, with less iron, and a trace of silica is also present in the nucleolus. Alexander and Myerson (1937, 1938), who have recently examined the nerve fibre by this method, find no ash in the myelin sheaths and only a trace of bluish ash which volatilizes at about 650° C. in the axis cylinder. This may be magnesium. They found that the cells of the sheath of Schwann and the endoneurium of peripheral nerves contained mineral ash. In the central nervous system the nerve fibres left no ash, although lines of ash might be seen running along them which appeared to correspond to the processes of neuroglial cells.

Alexander (1938) showed that there was a considerable variation in the amount of ash left by different types of nerve cell. In general granule cells

contained denser mineral deposits than the larger nerve cells, but variations were also seen between different collections of granule cells. Those of the cerebellar cortex and of the fascia dentata were particularly rich in ash, while those of the cerebral cortex were poor. Differences also existed between different regions of the cortex ; thus the pre-central gyrus contained much more ash than the post-central, and the basal ganglia were very poor in mineral constituents. This work indicated a new method of approach to the study both of normal and pathological nervous tissue which may prove of considerable value. The method, however, fails to show the distribution of magnesium, a metal in which the nervous system is particularly rich but which is sublimated by the temperatures needed to ash nervous tissue satisfactorily.

The Structure of Nissl Bodies.—While photography of fresh cells by ultra-violet light has settled the vexed question of the pre-existence of Nissl granules and micro-chemical methods and micro-incineration have determined their chemical structure, it still remained doubtful to what extent their appearance in stained sections was determined by the fixative used. Cowdry (1932), for example, recently stated that the size and shape of the granules depended on the composition of the fixative. Nissl and the German school have always insisted that no interpretation of the appearance of nerve cells by the Nissl method was satisfactory unless the material were primarily fixed in alcohol. On the other hand, in England it has long been considered that the appearances after fixation with formalin were identical with those seen after alcohol, and that a variety of stains, including various hæmatoxylin lakes, could be used to demonstrate the Nissl granules in addition to the basic blues used by Nissl.

The recent work of Einarson (1935) seems to have disposed of this question. Using the new dyes, gallamin blue and gallocyanin, he was able to stain Nissl granules after any form of fixative and found the pattern and form of the granules to be essentially the same whatever the fixative used. It was shown long ago by Mackenzie (1897), Macallum (1898), and others that the Nissl granules contained iron ; and the presence of nucleic acid was shown by the application of Feulgen's technique. Einarson found that the acid dye gallamin blue stained the cell diffusely, leaving the nucleus and Nissl granules unstained in material fixed in ammoniacal alcohol, whereas after fixation in neutral alcohol or formaldehyde or in any acid or acid combination of fixatives this stain gave a picture similar to that obtained by Nissl's method. He therefore concluded that there was in the Nissl bodies an acidophil substance as well as a basophil one. Further, he showed that 24 hours' washing in warm water after fixation in 96 per cent. alcohol removed part of the basophil substance, leaving the acidophil substance unchanged. From this work he formulated two conclusions. First, that in the perikaryon there are two substances in a colloidal state : (*a*) a fluid which represents the dispersed phase and after coagulation forms the Nissl bodies, and (*b*) a viscous semi-solid or plastic substance which forms the continuous phase and conditions the typical formation of the pattern of neurofibrils. Secondly, that the Nissl bodies have three constituents, a basophil chromatin substance, a basophil protein, and an acidophil protein. Of these, the first

two are soluble in acids (and in sodium carbonate after fixation) and the second is soluble in warm water.

Mitochondria.—The presence of mitochondria in nerve cells was for a time disputed, but has been established by Cowdry (1912, 1914) and many recent workers who have applied the supra-vital technique with Janus green and other modern staining methods. The early failures to stain mitochondria selectively appear to have been due to the rapidity with which they disappear after death and to the need for special fixation for most of the histological methods. In normal cells they occupy the same position as the Nissl granules. Bertrand (1927) and Bertrand and Hadzigeorgiou (1928), who studied them by infra-red photography, found that they retained this position in chromatolysis and might even remain unchanged after the Nissl granules, disappeared, as for example in Landry's paralysis. Choja (1936) recently made an extensive study of the mitochondria and found considerable differences between nerve cells of different systems in the number of granules present. In general, the pyramidal cells of the cortex and the sensory nerve cells of the brain stem, spinal cord, and dorsal root ganglia contained more than the motor nerve cells of the brain stem and spinal cord ; the Purkinje cells of the cerebellum and the cells of the vagal nuclei contained abundant mitochondria, while the cells of the cornu ammonis were very poor in them. In inflammatory, toxic, and virus diseases of the nervous system, the mitochondria rapidly altered, becoming at first larger and more numerous, but soon shrinking and disappearing as the disease progressed. In many cases he found a tendency for a particular organism or virus to affect the mitochondria of particular groups or systems of nerve cells. Whether this " selective vulnerability " of the nerve cells is due to differences in the mitochondria or in some other constituent of the nerve cell is not, of course, shown by this study, since it is probable that mitochondria are to a great extent dependent on the general health of the cell. For example, Weston Hurst (1929) found in poliomyelitis that, although the mitochondria in the affected cells of the anterior horns disappeared less rapidly than the Nissl granules and might still be present in the earlier stages of neuronophagia, they did not survive the death of the cell. Marinesco (1930) and Bertrand and Hadzigeorgiou (1928) considered that mitochondria granules, by breaking down, gave rise to lipochrome. This view was based not only on similarity of chemical structure, but also on the observations of the latter workers that cells containing much lipochrome contained few or no mitochondrial granules. This relationship was specially noted in senile dementia and in amaurotic family idiocy. This theory is attractive, but more work is needed before the relation of these constituents of the nerve cell is finally established.

All this work has done little to alter the conception of the nerve cell formulated by Cajal and Nissl. Rather it has confirmed their work by indicating the presence in the living cell of structures which, allowing for the inevitable results of fixation, have the characteristics of the neurofibrils and basophil granules which they described. The modern conception of the nerve cell is that its protoplasm is remarkably firm and static, perhaps a pre-requisite for its long life. On the other hand, its cell membrane, if any exists, is extremely

tenuous, a character no doubt related to the extremely high rate of metabolism which nerve cells have been shown to possess, and to their extreme vulnerability when their environment is altered.

The Nerve Fibre

Normal Constitution.—The axis cylinder in the peripheral nerves of the frog has been subjected by De Renyi (1929, 1932) to examination by the micro-dissection method. The living axone consists of thick internodal segments separated by short, thinner segments at the nodes of Ranvier. According to De Renyi, the diameter of the living axone is about seven times the thickness of the myelin sheath along the internodes. Nageotte (1911) had shown that under the action of various fixatives, such as silver nitrate and formalin, the myelin swelled at the expense of the axone especially in the internodal segments so that in preparations fixed in this way the nodal part of the axone became thicker than the internode. After fixation with osmic acid the appearances corresponded more closely to those seen in unfixed nerves. De Renyi explained this by supposing that under the action of the slower fixatives, fluid passed out of the axones into the myelin sheath along fine pores between the two. But that the connection of axone with myelin sheath was not very intimate was shown by experiments in which he either injected fluid between the two, or pulled the myelin sheath away from the axone. Under such treatment, the outer surface of the axone was revealed as a smooth membrane from which the myelin could be lifted up or peeled off. A valuable part of his experiments had to do with the structure of the node of Ranvier. Here, as has already been seen, the axone is thinner but firmer than in the internodal part, and is less changed by fixatives. These characters persisted when the axone was deprived of myelin and sheath of Schwann, and appeared to depend on a difference in structure of the axone itself at this point. By careful micro-dissection after fixation in silver nitrate he was able to divest the sheath of Schwann of its close investment of endoneurium, or sheath of Key and Retzius. When this was done the cement substance at the node was found to come away with the endoneurium, leaving the sheath of Schwann as a continuous membrane apparently of syncytial character, an appearance which agrees well with its behaviour in degeneration of nerves.

As to the relative thickness of axone and myelin sheath, much has been written in the past. Older writers (Donaldson and Hoke, 1905) considered that the areas on cross-section of the myelin sheath and of the axis cylinder were the same. This would mean that the diameter of the axone was about five times the radial thickness of the myelin sheath. These estimates were made from nerves fixed in osmic acid in which the relative thickness of myelin sheath and axone might have been altered slightly. Arnell (1936) attempted to study this in a more direct manner by cutting frozen sections on the chilled knife and transferring these directly to the slide, where they were examined either with or without fixation and staining. He found that the ratio of the area of axone to myelin sheath was on the average 1 to 3·5, but was very variable. The lowest ratio in all nerves was 1 to 1 ; the highest was 1 to 6 in the largest fibres, 1 to 15 in medium-sized fibres, and 1 to 12 in the smallest fibres. It seems

doubtful, however, whether the method is sufficiently free from artefact for these results to be accepted at their face value, since it is unlikely that such great variation in the relative thickness of axone and myelin sheath exist in normal nerve fibres. It had previously been shown by Duncan (1934) that, except in the autonomic system, myelination was dependent on axone thickness, so that every axone in the spinal roots which was more than 1μ thick became invested with a myelin sheath. This observation may explain the large number of unmyelinated fibres in the peripheral nerves of smaller animals, such as the rat and cat, and their paucity in the human. So far, apart from some indication in the work of Arnell, there is little evidence that the relative thicknesses of myelin sheath and axone differ in nerve fibres with different functions.

The experiments of Perdrau (1937) on the diffusion of solutions up axis cylinders are of interest from the indications they give as to its physical nature. In the living rabbit, as well as in the excised nerve, he found that if the cut end of the sciatic nerve were bathed in Ringer's solution containing either methylene blue or acid fuchsin, the dye travelled up the axis cylinders at first rapidly, but afterwards more slowly, passing up a distance of 4 or 5 cm. in about 4 hours. The largest fibres stained most easily, and the intensity of the colour diminished the further the dye travelled. With the perineurium intact and the end of the nerves sealed off, no staining of the axone was obtained, so that it was clear that the dye reached the axone at its cut end and passed along it. Kataphoresis was found to facilitate the passage of the dye, and after it the axone stained more deeply. If the nerve were bathed in a mixture of iron ammonium citrate and potassium ferro-cyanide the solution passed both up the nerve and along the connective tissue sheaths and, after fixation in acid formaldehyde, Prussian blue granules could be demonstrated in the cement substance of the node of Ranvier as well as in the axis cylinder. A picture closely resembling the cross obtained by Ranvier's silver method was thus obtained at the nodes.

A remarkable result was obtained when the iron ferrocyanide solutions were made by kataphoresis to travel up the nerve into the spinal cord. In these experiments many of the nuclei of the anterior horn cells were stained, leaving the nucleolus and the chromatin unstained. The nerve cells in the dorsal root ganglia, however, remained unstained. Perdrau had not suggested that the axone had a more direct relationship with the nucleus than with the perikaryon, but the analogy between his experimental results and the observations made by Hurst (1936) and others on the effects of neurotropic viruses on the nerve cell are striking (*v. infra*).

The axone may therefore be considered as a protoplasmic thread containing a more fluid part, the axoplasma, and fine, very delicate threads of a firmer consistence, the neurofibrils. The fact that slow fixation causes less shrinkage at the nodes of Ranvier than at the internodes is best explained by supposing that the axoplasma is less fluid in the nodes than in the internodes as it seems unlikely that the neurofibrils differ in consistency in different parts of the nerve fibre. That the axone is surrounded by a delicate membrane seems established by the work of de Renyi, but whether this membrane is derived from the sheath of Schwann, as in the older conception of the sheath, or whether it is an

integral part of the axone remains undecided. The latter appears the more plausible hypothesis, as the character of the axone appears to be the same in the central nervous system as in peripheral nerves.

Nerve Regeneration.—The debatable ground between physiology and pathology, represented by the regeneration of peripheral nerves after section, was very fully explored by Cajal (1913–14, 1928), especially in the researches which he made in his later years to disprove, once and for all, the catenary theory of nerve regeneration. This subject has been studied in the living nerve by Peterfi (1931) and Speidel (1935), who used young tadpoles at a stage when their tails were sufficiently translucent to allow of microscopic investigation with high microscopic powers. Many details of possible variations from the usually accepted methods of regeneration were thus brought to light. Speidel emphasized the symbiosis of axone and sheath cell, showing that sheath cells which lost their nerve fibre rapidly disappeared. Whether this occurs in adult mammals is doubtful, as the band of Büngner is preserved for long periods after nerve section, and the rate of growth of new axis cylinder sprouts, when they reach the bands of Büngner in the peripheral segment of a cut nerve, does not appear to be reduced when regeneration is delayed for weeks or months. Speidel found that the growth of the axone might be stimulated by such factors as the proximity of the growth cone of another axone or by mitosis in the sheath cell or in a neighbouring myoblast, which might result in the formation of a lateral branch from the axone. He found in the living, as Dustin (1910) deduced from the study of fixed material, that the orientation of the growing nerve sprouts was largely determined by the growth of fibroblasts, the constant movement of which swayed the growth cone about or bent the axone.

Among the most interesting of his observations was that, in regenerating nerve fibres, myelin might be formed in an internodal segment separated from the normal nerve (from which the fibre arose) by one or more unmyelinated segments. Whether this is a usual process in the regeneration of human nerves has not yet been established. In a case of section of both the sciatic nerve and the popliteal artery by gunshot wound which I examined some years after the war, I found the unusual condition of regrowth of numerous axis cylinders into the peripheral segment of the nerves with little or no attempt at remyelination. This was attributed to the very inadequate blood supply to the peripheral part of the limb. It is thus possible that local conditions of nutrition may determine whether or not individual segments of regenerating nerve fibres become myelinated.

It is difficult to assess to what extent this mechanical or hydrodynamic theory of the orientation of nerve sprouts cuts across Cajal's theory of neurotropism, as Cajal accepted it as a partial explanation of the path taken by nerve sprouts in a stump neuroma or junction neuroma. In his later papers he considered that neurotropism, i.e. a chemical attraction by substances formed by the cells of the sheath of Schwann or band of Büngner, only came into play when the nerve sprouts approached the ends of these bands. There has been and can be little question that as soon as the nerve sprouts enter the band fibres they take on a much more rapid and harmonious growth. This has been shown repeatedly in human cases of nerve section and suture as well as in animal experi-

ment. But the author's observation of human material, as well as a careful reading of the experimental results of Cajal and others, suggest that the word " neurotropism " is too strong for the factors at work, which seem to be more nutritive than attractive. It is clear that the growth of nerve sprouts is stimulated when they come into contact with or in close proximity to sheath of Schwann cells derived from the same animal or an animal of the same species, whereas their growth is inhibited by sheath of Schwann cells from other animal species and by most other kinds of tissue, whether homologous or heterologous. The point at issue is rather the distance at which this nutritive action works and whether the orientation given to growing nerve sprouts depends on a chemical attraction or on more mechanical factors.

Nageotte (1914) has demonstrated, and experience in cases of nerve section has repeatedly confirmed, the formation of outgrowths of " band fibre " nature from the peripheral cut end which may unite with nerve sprouts from the proximal end, or may form a stump neuroma which contains no nerve fibres. In either case the arrangement and direction of the outgrowths of band fibres appears to be determined chiefly by the fibrous and other tissues which surround them, and the junction of an empty band fibre with a nerve sprout seems to be determined largely by chance aided by the orientation of collagen fibres along lines of tension.

Neurone in Disease

Axonal Reaction

The well-known reaction of the nerve cell to injury or disease of its axone has been so thoroughly studied by Nissl that it would seem that little fresh could be gained in this field. Further studies have, however, added something to our knowledge of this reaction. Penfield (1920) applied Cajal's method for staining Golgi's internal apparatus to nerve cells after section of their axone, and showed that the changes in this structure were analogous to those in the Nissl granules, but differed in certain respects. For example, while the Nissl granules in the cells of the dorsal root ganglia showed little change after section of the dorsal roots, the Golgi apparatus was definitely altered. This change began on the 4th day and reached its zenith by the 7th day after nerve section. In the anterior horn cells after section of the sciatic nerve it appeared on the 7th day and had reached its maximum on the 12th day.

Nicholson (1923–4) studied the cells of the hypoglossal nucleus in rats, after section or tearing out of one hypoglossal nerve, by Macallum's hæmatoxylin method for iron, and showed that the masked iron in the Nissl granules disappeared along with the Nissl granules. The loss of chromophilic substance was thus associated with a change of chemical composition in the cell. When the hypoglossal nerve was torn out the iron disappeared gradually, first from the cytoplasm and later from the nucleus, so that by the 35th day the cell was completely deprived of iron. Such cells were considered dead. In the less severe degrees of reaction iron appeared to pass from the nucleus into the cytoplasm of the cell, especially towards the axone hillock, but it never entered either the axone hillock or the axone itself.

Transneuronal Degeneration

Further study has also recently been given to the question of transneuronal degeneration of nerve cells. Mott (1911) gave a negative answer to this question, stating that though " direct injury " of any part of the neurone would cause changes in it, injury of neurones with which it was functionally, but not nutritionally, connected would have no effect on it. When both sciatic nerves of an animal were cut and hemi-section of the cord also made, he could find no difference in the degree of axonal reaction on the two sides of the cord. This was in opposition to the previous findings of Marinesco (1909) and others. Recent work has, however, given indisputable proof that transneuronal degeneration may occur, at least in certain systems. Minkowski (1920) was the first to observe atrophy of certain cell layers in the external geniculate body after lesions of the optic nerve. He described the reaction as a shrinkage of the cell body without other evidence of degeneration. Le Gros Clark (1932) found a similar atrophy in a middle-aged woman two years after enucleation of one eye, and in a macaque monkey seven months after destruction of an eye. He describes the cells as shrunken and chromatolytic. With Penman (1931) he used this reactionary atrophy in experimental studies of the relations of areas in the retina to the cell layers in the external geniculate body. Horanyi Hechst (1933) and Balado and Francke (1937) have also observed laminar atrophy in the external geniculate body in cases of optic atrophy resulting from the pressure of tumours.

We are dealing here with cells which probably do not receive synapses from any neurones other than those coming from the retina, and which for that reason may be especially sensitive to lesions of the optic nerve. But Foerster and Gagel (1934) after section of the dorsal roots have demonstrated a chromatolytic reaction in the secondary afferent neurones of the spinal cord as well as in the motor cells of the ventral horns and in the intermedio-lateral tract. The demonstration of degenerating " boutons terminaux " round the same neurones proved that they were in direct synaptic connection with the primary sensory neurones. This transneuronal reaction was found to begin 6 days after section of the roots, and might still be visible 6 months later. These neurones, at least the ventral horn cells and the intermedio-lateral tract, are in connection with one or more neurones other than those severed by the operation. A similar reaction in the ventral horn cells may sometimes be seen in cases of cerebral tumours involving the precentral convolutions. It is probably much more common than has been supposed, and it may be of considerable importance in human pathology, for example in the pathogenesis of system diseases such as amyotrophic lateral sclerosis and the cerebellar degenerations. The swelling of the cells of the inferior olive after lesions of the central tegmental tract in the pons, described by Foix, Chavany, and Hillemand (1926) and others, is a case in point.

Ischæmia and Anoxæmia

Ischæmic Changes in the Nerve Cell.—" Ischæmic " changes in the neurone are such common and well-known findings in human pathology that they

would seem scarcely worthy of discussion were it not that some controversy has arisen on the interpretation of histological changes found in certain diseases as due to anoxæmia. In human pathology it is obvious that the effects of post-mortem autolysis must be the same as those of the earlier stages of ischæmia, and consequently the greatest care has to be taken in the interpretation of these changes. In animal experiments another complicating factor arises. It is common knowledge that when animals are killed and their nervous system placed in fixative within a few minutes of death, the nerve cells, especially in the cortex, assume two very different forms : some appear swollen and pale, others shrunken and hyperchromic. It is assumed that these differences depend on the state of activity of different neurones at the time of death. In reviewing the literature of experimental work it is remarkable how frequently this normal finding has been interpreted as being related in some way to ischæmia, and in consequence many of the results must be accepted with caution.

There is little doubt that Nissl's " chronic cell change " may be produced by ischæmia, though whether this is its only cause may be open to question. Gildea and Cobb (1930) and Tureen (1936) have made fresh experimental studies, and their results, especially those of Tureen, are of considerable interest. All experimenters have shown that there are considerable differences in the resistance of different nerve cells to ischæmia. Gomez and Pike (1909), for example, gave the following order of vulnerability : (1) the smaller pyramidal cells of the cortex ; (2) the Purkinje cells ; (3) the cells of the medulla, retina, and spinal cord ; (4) cells of the spinal root ganglia. As to the duration of complete cessation of blood flow required to produce any lasting change in the nerve cells, there is less certainty as it is probable that in all experiments on the brain a very slight flow of blood is still present in the cortical capillaries. Gildea and Cobb observed such a flow ophthalmoscopically in their experiments, however many of the main vessels to the head and neck were obstructed. They concluded, however, from their own experiments and those of Ford (1928), who had used the method of replacement of oxygen by nitrogen, that the cortical neurones may be irreparably damaged after 5 minutes of anoxia or severe ischæmia. The medullary neurones may survive up to 20 or 30 minutes of almost complete cessation of blood supply, and according to Tureen (1936) complete stoppage of the blood flow to the spinal cord may be recovered from if it lasts less than 20 minutes. In addition to the well-known " chronic cell change " of Nissl, Gildea and Cobb describe an early stage in which the nerve cells stain diffusely and have spike-like dendritic processes, and a later stage, only seen in animals surviving for 48 hours or more, in which the nerve cells appear somewhat swollen. Although liquefaction of nerve cells was never seen, many of the cells, particularly those of the third and fourth cortical layers, had disappeared in 24 hours after temporary ischæmia, producing " areas of devastation " or " areas of pallor " which were identical with those on which Spielmeyer (1930) has laid so much emphasis in human pathology.

Tureen's experiments were conducted on the spinal cord of cats. He found that when he clamped the thoracic aorta just below the arch and then injected

neutral red into the circulation, there was no staining of the lower thoracic and lumbar cord, thus showing that the blood supply to these areas had ceased. In a large series of experiments the aorta was clamped at this level for periods varying from a few minutes up to 1½ hours, and the animals were kept alive for from 1 hour to 4 months. He found that all animals in which the aorta was clamped for 20 minutes or longer remained permanently paralysed in their hind legs, whereas those in which it was clamped for 15 minutes or less recovered within 24 hours. The sequence of changes in the motor neurones of the lumbar cord was carefully studied in these animals. The nerve cells were all affected, though the degree of change might not be the same in all. In the experiments in which the animals recovered, extensive loss of Nissl granules was seen 7 hours after the experiments. The cytoplasm stained deeply, and contained an amorphous deposit, with occasional traces of Nissl substance near the periphery of a few cells. Many of the nuclei stained deeply. At a rather later stage (28 and 36 hours after the experiment) the cell body and dendrites stained darkly ; the nuclei were still more deeply stained and might be eccentric. Some cells had a globoid shape, others retained their normal outline. At a rather later stage (48 hours) neuronophagia of some of the nerve cells could be seen. It is noteworthy that these changes were present at a time when all evidences of paralysis had passed off. Reparative changes in the neurones first made their appearance after about 72 hours, in a gradual reappearance of Nissl granules, usually first in the periphery of the cell. After 6 days the nerve cells had almost regained their normal appearance, but stained rather deeply ; at later stages they differed in no way from those of normal control animals. Of the experiments in which permanent paralysis was produced, those with 30 minutes' obstruction of the aorta were specially interesting. From 1 to 12 hours after these experiments, Tureen found swelling and rounding of contour in all the nerve cells. In the early stages this resembled the " acute swelling " which Marinesco (1909) had described in similar experiments ; it disappeared in 24 hours and was replaced by the shrunken hyperchromic appearance commonly associated with ischæmia.

These experiments appear to have been well controlled, and present an even series in which the results were predictable within certain limits. They are therefore important as indicating the degree of ischæmic change in ganglion cells from which complete recovery can take place. It is noteworthy that in the experiments with recovery of function the nerve cells showed neither early swelling nor later shrinkage, although the diffuse staining seen in the severer degrees of ischæmic degeneration was well marked.

In a later study of these spinal cords by the micro-incineration method Tureen (1938) observed alterations in the mineral deposits in the nerve cells which could not be fully correlated with the changes seen by Nissl's method. In the experiments in which the aorta had been compressed for only 15 minutes there was a progressive increase in minerals both in the nucleus and in the cell body, especially towards its periphery. This attained its maximum in 36 hours and persisted for 2 weeks or longer. In the experiments in which the ischæmia was continued for 20 minutes or more, a transitory stage of hypermineralization

gave way after 1½ hours to a stage of progressive loss of minerals, so that at the end of 13 hours the nerve cells might contain no more minerals than the surrounding tissues, although in some cells irregular dense deposits of minerals were seen even in the later stages of cell dissolution.

In human pathology the slighter recoverable changes in nerve cells are difficult to distinguish from the results of post-mortem autolysis. But when they are found in limited areas related to an obstruction of the blood supply, either on the arterial or venous side, they are significant. Changes of this character, as well as of more severe degree, may be seen, for example, in the cortical nerve cells near a thrombosed cortical vein, in an area where the blood flow is greatly retarded. The more common result of ischæmia in human pathology is the disappearance of nerve cells which leave no trace except an overgrowth of neuroglia and microglia. This is often seen in localized " areas of paling " in the fourth and fifth layers of the cerebral cortex and characteristically also in Sommer's sector in the cornu ammonis. When Purkinje cells disappear in this way, as they often do, the phagocytic glial cells are arranged along the dendrites in an arrangement to which Spielmeyer gave the name " glial bush arrangement " (Glia-strauchwerke).

These local disappearances of nerve cells are so commonly seen in epilepsy that they have been considered characteristic of the disease, although they may also occur in poisoning from carbon monoxide and nitrous oxide and have been described as occurring in cases of hypoglycæmic coma without convulsions. All these conditions are akin to ischæmia in that they interfere with the metabolism of the nerve cell. Whether in epilepsy the death of nerve cells should be ascribed to the intense congestion and capillary stasis which occurs during the fit or to a spasm of small vessels accompanying it is at present an open question. Spielmeyer (1930) has remarked that the areas which are especially liable to be affected derive their blood supply from rather long, fine vessels which lack the rich anastomosis which is present in less vulnerable areas of the cortex.

Ischæmic Changes in the Nerve Fibres.—Ischæmic changes in the nerve fibres have not been so fully studied experimentally, although they are well recognized in pathology. Tureen's observations on the spinal cord would indicate that the axones are less vulnerable to ischæmia than the cell body, as he did not observe any softening or degeneration in the white matter of the cord in his experiments. The local vacuolar swellings in the lateral columns of the spinal cord which are commonly seen in cases of epidural tumour are more likely to be due to ischæmia than to direct pressure, as their appearance is similar to that seen at the margins of the softened area in cases of thrombosis of the posterior inferior cerebellar artery. They usually lie at a little distance below the surface in the lateral columns, although they may occur further forward. They appear to occur very rarely in the dorsal columns. Quite frequently they are related to a small vessel. They are most often seen in cases in which paraplegia has recently become fairly complete and probably represent the most severe effects on the cord of an ischæmia which is interfering considerably with the function of all the tracts.

Cerebral Œdema

Closely related to ischæmia is the problem of œdema, and from the point of view of pathogenesis any sharp distinction between them is artificial, since œdema also probably interferes with the oxygen metabolism of the neurones. It is not surprising, therefore, to find similar changes in the nerve cell in œdematous areas of the cortex as are seen in the milder grades of ischæmia. Most often the cells are shrunken and stain homogeneously, showing a minor degree of Nissl's chronic cell change. The more severe degrees of this change from which recovery is impossible are less often seen.

The writer has recently, with M. L. Miller, studied the effects of œdema on the white matter of the brain. Local œdema, such as is seen near a tumour or abscess of the brain, appears to affect the centrum semi-ovale more than the cortex. Its effects are certainly more obvious in the white matter, and often cease near the cortex, sparing the subsulcine layer of fibres. These effects consist not only in a separation of the nerve fibres from one another, but in a general impoverishment of the myelin sheaths, which tend to be irregularly beaded and show here and there " sudanophil " droplets. When œdema is very marked, as after severe injuries with fracture of the skull, areas of complete demyelination may be found. This is unusual, but in all except the mildest grades the area of œdema is demarcated in Weigert-Pal preparations by a diffuse pallor which cannot be altogether attributed to separation of the nerve fibres by interstitial fluid. While the myelin suffers obvious and irreparable damage, the axones do not escape, but show varicosity, irregularity of outline, or the formation of end-bulbs in varying degree. These changes for the most part seem to disappear along with the œdema. They are at least much more obvious in œdematous areas than in areas showing pallor of the myelin from which the œdema has disappeared. The local areas of demyelination of the centrum semiovale, which may be found months or years after a severe cerebral contusion, are probably attributable more to the œdema which follows the injury than to the blow itself, although the local bruising of the cortex will entail some loss of fibres underneath it and hæmorrhage into the white matter may account for some loss of myelin.

Avitaminosis

The neurone is particularly liable to be affected in conditions of avitaminosis. It would probably be wrong to consider that lack of any of the known vitamins affects the neuron alone, since in every case there seems to be some disturbance in general health. But the complex known as vitamin B appears, from the work of Peters (1936) especially, to be so closely linked with the metabolism of the nerve cell that its absence leads rapidly to a loss of function and, at a later stage, to changes in the structure of the nerve cell and fibre. The relation of the thermolabile factor B1 to degeneration of the peripheral nerves is so well known as hardly to call for comment were it not for the very careful and detailed observations which have recently been made by Bertrand, Liber, and Randoin (1934). These authors fed pigeons on a carefully balanced diet deficient only

in B1 and killed them for histological study at various stages of the resulting paralysis. They found that the changes in the nervous system were confined to the peripheral parts of the sensory-motor nerves, the unmyelinated autonomic nerves remaining intact. They describe three types of parenchymatous change in the peripheral nerves : (1) one in which the axis cylinder appeared to be primarily affected ; (2) a simultaneous change in the myelin sheath and axon associated with separation of the myelin sheaths from one another at the nodes of Ranvier ; and (3) a form in which the most striking feature was the formation of varicosities and buds in the contour of the myelin sheath. Up to a certain stage these changes were comparable to those seen in Wallerian degeneration ; but after the early stages in which the myelin began to stain with the Marchi method, little further katabolism of myelin took place. Thus at the stage when it had broken up into hollow balls (containing fragments of axon), there was still no tendency to stain with Sudan. This delay in katabolism, after the fragmentation of the axon, was associated with a remarkable quiescence of the cells of Schwann, which did not form Erzholz bodies or undergo mitotic division and apart from a moderate increase in the amount of protoplasm remained inert. Nor was there any invasion of the nerve fibre by mesodermal phagocytes. When vitamin B1 was added to the diet the picture rapidly changed. The sheath cells underwent mitosis and increased in number, and phagocytic cells invaded the nerve fibre in which the lipoid droplets had become Sudanophil. It appeared likely that the arrest of katabolism of myelin at the pre-Sudanophil stage was due to a direct metabolic disturbance in the cells of the sheath of Schwann rather than to any change in the composition of myelin induced by lack of vitamin B, otherwise it would be difficult to explain the rapid appearance of the usual picture of Wallerian degeneration after treatment.

This failure of activity in the sheath cells may be compared with a similar inactivity in them, amounting sometimes to necrobiosis, observed by de Villaverde (1926) in experimental lead poisoning.

The relation to nervous disease of the thermostable fraction of vitamin B (B2 or G) has never been so clear as that of vitamin B1. Goldberger and his associates (1928) produced in dogs a diseased condition associated with black tongue which they thought was closely similar to human pellagra, but they did not reproduce the nervous lesions of the human disease. Stern and Findlay (1929) in rats produced a similar condition associated with lesions of the epidermis and some degree of paralysis, but without definite changes in the peripheral nerves or tract lesions in the spinal cord. Zimmermann (1937), however, by a carefully balanced diet from which vitamin B2 was excluded, produced in dogs a subacute or chronic disease associated with loss of weight, vomiting, and diarrhœa, and great muscular weakness and ataxia, but without " black tongue." In dogs on Goldberger's diet which developed " black tongue " only slight degeneration was found in the peripheral nerves and dorsal columns in the animals that lived longest. But in the more chronic disease the degeneration was very marked, both in the peripheral nerves and dorsal columns. The similarity of these changes to those seen in cases of pellagra is further

evidence of the relation of this disease to lack of vitamin B2, although several differences between the human and the experimental disease still remain. For example, Zimmermann insists that the anterior horn cells and Betz cells in his dogs were normal, whereas in the human disease the latter cells constantly suffer, along with many other cortical pyramids, from the chromatolytic changes which Adolf Meyer called " central neuritis." On the other hand Stern and Findlay found changes in the neurones, but none in the tracts of the cord or peripheral nerves in rats deprived of B2 vitamin.

In the human disease the long tracts of the cord may or may not be affected. Usually the dorsal columns are more affected than the antero-lateral columns, but in a case reported by Langworthy (1931) the reverse was the case. In the specimens examined by the writer the degeneration appeared to differ from that of subacute combined degeneration in showing very little evidence of vacuolation in the early stages. It seemed to be a true Wallerian degeneration, and in the dorsal columns was related to degeneration of the entering spinal roots. In some of Pentschew's (1929) cases in which the duration of the illness was longer, asymmetrical areas of sclerosis were found on the margins of the antero-lateral columns.

The relationship of vitamin A to diseases of the nervous system is less clear, although certain observations lend strong support to it. Mellanby (1931) seems to have been the first to produce definite degeneration of the spinal cord in dogs by diets deficient in this vitamin. He found that a more rapid development of paralysis and more definite changes in the spinal cord were seen when, along with deprivation of A, the animals were given whole wheat or rye. Still earlier and more striking evidence of cord degeneration was obtained by the addition of ergot to the diet, an observation which falls well into line with the well-known occurrence of degeneration of the spinal cord in epidemics of ergotism during years of famine. These results have been confirmed by Zimmermann and Burack (1934) in young white rats, which, in addition to the loss of weight found by all observers in rats deprived of vitamin A, suffered from inco-ordination and sometimes paralysis of the hind limbs. In these animals they found degeneration of both sciatic nerves and brachial plexus, in the dorsal, and sometimes in the ventral, roots and in the dorsal columns and the margins of the ventro-lateral columns of the cord. The degenerations in the spinal cord were not cured by carotin, nor did this substance prevent them unless given in adequate doses from the beginning of the experiment.

Eveleth and Biester (1937) have observed a disease in swine called " posterior paralysis " and associated with myelin degeneration in the cord and peripheral nerves. These animals were on a diet in which vitamin A was low, but was not completely absent. They have confirmed Zimmermann's observation that once paralysis had set in it was not cured by cod-liver oil. But in reviewing the evidence they were not satisfied that the degeneration in the cord was due entirely to a lack either of vitamin A or of the vitamin B complex, and postulated, as Mellanby has done, some toxic or positive factor as well as lack of vitamins.

In other food-deficiency diseases in which the spinal cord undergoes degeneration we are on less certain ground, as it is not known to what extent one

of the known vitamins may be at fault in addition to the food element which is potent in curing the disease. In this country the most common of these is *subacute combined degeneration* of the cord. There is so far no certain evidence that this condition ever occurs apart from a megaloblastic anæmia curable by liver or liver extract, i.e. Addisonian anæmia, and it has become increasingly evident during the past few years that preparations of liver, if given in sufficient dosage, produce amelioration often amounting to cure of the nervous symptoms.

The degeneration in the spinal cord appears to affect the myelin earlier than the axis cylinders, although the latter never escape degeneration for long. It consists in the early stages of fusiform swellings of the nerve fibre in which the myelin is stretched round a vacuole which forms between it and the axis cylinder. At this stage the myelin retains its double refractility with a myelin cross and stains well by hæmatoxylin lakes. More than one swelling may be seen on the course of a nerve fibre in longitudinal sections. The axones may lie centrally or toward one side of the vacuole and often show varicosities or irregular swellings, presaging early dissolution. But it appears that if the disease is arrested at this stage or even after actual katabolism of myelin has begun, the axis cylinder may recover so that naked axones may be seen in sclerotic areas. The degeneration of the central parts of the dorsal columns described by Michell Clarke (1904) in pernicious anæmia appears to be the commonest early stage of the disease (Greenfield and O'Flynn (1933)). That the peripheral nerves are also affected in most, if not in all cases, was suggested by Russell, Batten, and Collier (1900) in their classical paper, and was confirmed by Greenfield and Carmichael (1936). The latter found in the terminal nerve twigs to the toes a condition of loss of myelin, apparently without corresponding lesions of the axis cylinders and without any of the severe degenerative changes commonly seen in polyneuritis.

Our knowledge of this curious disease may be carried a stage further by evidence gained from a similar condition which has been found in monkeys in captivity by Perdrau (1930) and Hamerton (1936–7) in this country, by Levaditi, Lepine, and Schoen (1930) in France, by Schob (1931) and Scherer (1932) in Germany, and by Davison (1934) in Germany. In these monkeys either the spinal cord or the brain or both may be affected, and in some animals there has also been degeneration of the optic nerves. Degeneration of the white matter of the brain in the form of discrete patches has been observed in many cases of subacute combined degeneration, but in that condition it is rare and seldom severe. For this reason the degeneration found in the brains of monkeys was at first thought to resemble most closely the lesions of diffuse sclerosis or Schilders disease. But both Hamerton and Scherer (1937), who have been able to study many examples of varied severity at all stages of the disease, have no doubt that it is most closely allied to subacute combined degeneration of the cord. That it may be caused by a vitamin deficiency or unbalanced diet is suggested by Scherer's monkeys, in which the nervous symptoms came on after a severe epizootic of diarrhœa or dysentery from which many died.

Whether the degeneration in the spinal cord of these monkeys shows a histological picture identical with that seen in subacute combined degeneration

remains unsettled. It has been too readily assumed that all forms of combined degeneration of vacuolar type which show little tendency to be limited to definite tracts in the cord must be closely related to one another, both in their finer histological details and in their ætiology. In the present state of our knowledge that assumption does not seem altogether warranted. Nor should the analogy between " cage paralysis " and subacute combined degeneration of the cord be over-stressed. The monkeys do not all have achlorhydria, and the disease may undergo spontaneous remission with some recovery, a condition rarely seen in subacute combined degeneration before the days of treatment with liver.

Neurotropic Viruses

Much study has been devoted during recent years to the mode of attack by neurotropic viruses on nerve cells. Their grosser effects in causing total destruction of the cells, either with or without neuronophagia, has been known for many years, and the older conception of a primarily inflammatory or vascular reaction with secondary affection of the neurone has been entirely abandoned. In rabies this newer view is old enough. It was indicated by the discovery by Negri (1903) of the inclusion bodies characteristic of the disease, and was established by the classical studies of Achucarro (1910). In the epidemic of encephalitis lethargica it soon became evident that certain systems of neurones, especially those of the substantia nigra, were primarily affected and often degenerated rapidly and disappeared without neuronophagia and with comparatively little inflammatory or vascular disturbance in their neighbourhood. Later studies of Borna disease by Nicolau, Dimanesco-Nicolau, and Galloway (1929), of poliomyelitis by Weston Hurst (1929–31), and of other virus diseases of the nervous system, have not only confirmed this view, but have added many histological details indicating the manner in which the neurone is attacked.

Achucarro's studies were remarkable both for their completeness and also for the accuracy with which he described changes in the neurone which have been found to be common in greater or less degree to all diseases caused by neurotropic viruses. In addition to giving a fuller description of the inclusion bodies which Negri had described, he studied the neurofibrils and the Nissl granules and gave the first description of the early changes in the nucleus. He confirmed Cajal's (1904*a*) finding of early thickening and later dissolution of the neurofibrils which Hurst later found also in the early stages of poliomyelitis. The early nuclear changes which he described consisted of swelling and diffuse appearance of the acidophil elements with fragmentation of the basophil chromatin. These changes might precede any obvious disturbance in the cell body. Later with the disappearance of the nuclear membrane various degenerative changes were found in the cell body.

Somewhat similar nuclear changes were described by Lipschutz (1921) and confirmed by Goodpasture (1925) in the nerve cells in experimental herpes encephalitis. In this disease the earlier stage of swelling and greater intensity of staining of the acidophil elements does not appear to progress to the formation of more definite intranuclear bodies. In poliomyelitis Covell (1930)

demonstrated the formation of small, strongly acidophil intranuclear bodies, and Weston Hurst (1931*a*) later confirmed this and described the various stages in their formation.

The intra-nuclear inclusion bodies described in Borna disease by Joest and Degen (1911) and later studied more extensively by Nicolau and Galloway appear to be of very similar origin, but differ from most other bodies of this kind in showing a clear halo round the oxyphil granules. Similar oxyphil intranuclear bodies have been described in yellow fever, pseudorabies, equine encephalomyelitis, and other forms of virus encephalitis in animals.

In all these diseases oxyphil intranuclear bodies are found only in cells which are relatively little affected, although they may show chromatolysis and other degenerative changes of the cytoplasm. In cells which are obviously dead and which are undergoing neuronophagia the nucleolus and chromatin have usually disappeared and the nucleus may stain diffusely with acid dyes, but no structures resembling inclusion bodies can be seen. In Borna disease Nicolau and Galloway postulated that the presence of inclusion bodies, indicated the victory of the nerve cell in its fight with the virus, and the finding by Hosselet and Erbes (1935) of inclusion bodies in a large proportion of the dorsal root ganglion cells in poliomyelitis supports this view. Hurst, however, is somewhat doubtful of its universal application, seeing that many nerve cells which contain nuclear inclusions are obviously degenerated.

Intranuclear inclusions may be single or multiple, according to the disease in which they are found. Those of Borna disease are often single, whereas in poliomyelitis, pseudorabies, and yellow fever they are always multiple. They are often associated with fragmentation of the nucleolus and margination of the nuclear chromatin.

There has been some controversy as to whether they are sufficiently specific to be regarded as evidence of the presence of the virus in the nerve cells, as somewhat similar appearances have been seen in brain tumours and many pathological conditions. Hurst (1934) has pointed out that these appearances can also be seen in normal nerve cells under special conditions of fixation and staining, but they differ from the true nuclear inclusions in appearing less solid and sharply defined and less brilliantly stained with acid dyes, and often also in showing little projections uniting them to the general, weakly acidophil, nuclear reticulum. " They never show evidence of internal heterogeneity, as do frequently the bodies described as nuclear inclusions." Nor do the nuclei containing them show other evidences of degeneration.

If nuclear inclusions are evidence of the penetration of virus into nerve cells we should expect them to bear some relationship to the better known cytoplasmic inclusions, such as Negri bodies. The origin of these had given rise to much controversy. They have been considered, especially by Levaditi and his co-workers (1926) to constitute a phase of the parasite Glugea Lyssæ. Goodpasture considered the smaller lyssa bodies and the acidophil part of the Negri bodies to arise from degeneration of the neurofibrils, and the basophil " inner bodies " from degeneration of mitochondria. However, a number of workers (Lentz, 1909 ; Benedek, 1921 ; Suzuki, 1930) have postulated an

origin from the nuclear sap. Marinesco and Stroesco (1931) found them to contain neither nucleic acid nor iron, which was definite proof that they did not constitute an intra-cellular parasite of the glugeid family. On the other hand, they found definite evidence that they were derived from the nucleus. They found in rabies nuclear inclusions very similar to those seen in other virus diseases, such as poliomyelitis and Borna disease, and postulated that these bodies passed through the nuclear membrane into the cytoplasm, where they enlarged into the typical Negri body.

Cytoplasmic inclusions have also been found by Weston Hurst (1931*b*) in mice infected with " louping ill," and in them at least no nuclear inclusions could be seen. Therefore, although Marinesco's theory of the origin of Negri bodies from nuclear constituents is attractive in bringing rabies into line with other virus diseases of the nervous system, it cannot be considered as proved. Covell and Danks (1932) do not support his findings otherwise, as they obtained a weak Feulgen reaction for nucleic acid in some of the Negri bodies, and saw evidence of iron in them in ashed sections.

The controversy that has raged round these bodies has been valuable at least in diverting attention from the obvious inflammatory changes associated with virus disease of the nervous system to the finer but more specific reaction which they cause in the nerve cell. As Spielmeyer (1929) has insisted, inflammatory and neuroglial reactions in the nervous system are limited in type and may be the same in diseases of very different ætiology, or may vary greatly from case to case in the same disease. To some extent this may also be true for the reactions of the neurone, but many of the changes seen in it are so closely related to the disease in which they occur as to be almost specific, e.g. the changes seen in such conditions as amaurotic idiocy, Alzheimer's disease, disseminated sclerosis, and subacute combined degeneration.

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A CASE OF APHASIA, WITH SPECIAL REFERENCE TO THE PROBLEMS OF REPETITION AND WORD-FINDING

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So much has been written on the subject of aphasia that the presentation of another case report requires some justification. The following case of amnesic aphasia was not only unusual in its clinical aspects, but also raised a number of important questions with regard to the phenomena of repetition and word-finding, and to the problem of cerebral localization of language function.

Case Report

G.B., a 56-year-old white man, was admitted to the Montefiore Hospital on 25th August, 1935, with a history of a " stroke " eight months previously, followed by sudden onset of unconsciousness and paralysis of the right side of the body. He recovered consciousness after about one hour, seemed quite clear mentally and was able to talk coherently. Six hours later, however, he developed difficulty in speaking, although he seemed to understand what was said to him. There was bladder and rectal incontinence during the first week, but not thereafter. After one month the motor weakness, especially of the leg, improved and he was able to walk about. The speech disability, however, persisted.

The past and family history were not important except that the patient's father had died of " apoplexy " at the age of 52.

The patient was a poorly nourished, elderly man, ambulatory, and not acutely ill. Heart sounds were regular, but of poor quality and there was a faint systolic murmur at the apex. Peripheral vessels were moderately thickened. Blood pressure was 130/84.

There was a right spastic hemiparesis, with the arm in extension. The leg was less involved than the arm. Deep reflexes were increased on the right, with right ankle clonus. Abdominals and cremasterics were all present, but markedly diminished on the right. Troemner, Babinski, Rossolimo, and other confirmatory signs were present on the right. There was a mild, right-sided hemisensory syndrome, including the face, extending to the left of the mid-line, and involving all modalities. Sensory impairment was greatest in the hand. There was also distinct hyperpathia on stroking or pinching the right half of the body. The pupils reacted somewhat sluggishly to light and accommodation. The fundi were normal. There was questionable impairment of vision in the right homonymous fields. The face showed a slight right supranuclear weakness.

Mental Examination.

1. General Behaviour.—The patient's behaviour was noteworthy. He sat quietly in a chair most of the day, took no part and showed no interest in the ward activities, and spoke not at all to his fellow-patients. However, in any situation which directly concerned him—this otherwise quiet, noncommunicative and passive individual, became animated, excited and overtalkative. He answered questions freely and co-operated to the best of his ability in all investigations. He would talk incessantly to the doctors, discussing his infirmities at great length, with much facial expression and show of emotion, laughing and crying alternately.

2. Speech.—From the history it was noted that the patient had been able to speak at least five languages fluently—German, English, Yiddish, Polish, and French. At the time of our examination, he was still able to use any of these media for expression, but favoured a combination of English, German, and Yiddish. His speech was best under conditions of emotional stress. At such times, he spoke fairly coherently and grammatically, utilizing a good vocabulary. Usually he uttered short, simple sentences which contained all types of words, although at times a subject or a verb might be misplaced. There was no paraphasia. There was a tendency to stereotypy and he frequently repeated himself. The striking thing, however, was that despite this relatively good conversational speech, he showed a complete inability to name objects or to repeat to command either letters, words or sentences. Although he might have just used a particular word or sentence in spontaneous speech, he was totally unable to repeat it to command a moment later. When asked to recite the numbers from one to ten, or the letters of the alphabet, or the days of the week, he could do so only if the first few were given to him. Then if asked to repeat one of the symbols he was unable to do so unless he recited the whole series. Thus, if after counting from one to ten, he was asked to repeat the number seven, he could do so only by counting consecutively from one to seven. Often, in his attempt to repeat a given word, he would utter other words, which invariably were related to the given word. Thus when asked to say " God " he could not do so, but would say " Himmel " (Heaven) ; for " children," he would say " family " ; for " hospital "—" Montefiore " ; for " window "—" glass," etc.

He could not name even the most familiar objects although he was usually able to demonstrate or explain the use of an object that was shown to him, and sometimes uttered the correct word in the course of his explanation. When asked immediately afterward to repeat the word, however, he could never do so.

He understood many words, obeyed simple commands, was able to point to certain parts of his body as named, and could put out his tongue when asked. He also seemed to understand simple conversational sentences, although he did not comprehend more complicated ones. His understanding was always better when the spoken words fitted the particular situation which he was experiencing at the time (see Protocol I).

3. Writing.—He was able to print out his name in Latin capitals, but could

not write any other words. He could write numbers, both single and double, to dictation, and was able to perform, in writing, simple arithmetic computations.

4. Reading.—He was able to read only his name and the heading of the *New York Times*. However, it seemed that this was not real reading but a recognition of familiar visual pictures, since he could not read single letters or words. He could not identify a spoken word with a written word.

He apparently recognized pictures of objects although he could not name them. Similarly, he was able to recognize objects placed in his hands (with eyes closed) and could demonstrate their use, without being able to name them.

6. General Intelligence, and State of Sensorium.—Conversations with the patient and various tests indicated that he retained a fairly good level of intellectual activity. His memory and judgement were only moderately impaired. He had definite appreciation of the fact that his speech was changed. Sensorium was intact, and he was oriented in all spheres. His reactions to concrete situations within his immediate environment remained fairly good.

In contrast to this, however, he was completely unable to adequately handle any situation which required a capacity for abstract conceptions (see Protocols II, III, and IV).

Laboratory Data.—Encephalography showed marked cortical atrophy, with moderate internal hydrocephalus. In one of the A.P. views there was clearly visible in the region of the left Sylvian fissure a large triangular collection of air with its base pointed outward. Gastric analysis showed free HCL of 66, total acid of 78. Stool was positive for occult blood. G–I series indicated the presence of duodenal ulcer. Wassermann and other routine laboratory data were negative.

Course in the Hospital.—Patient complained frequently of epigastric pain, and G–I series showed evidence of a duodenal ulcer, for which he was treated medically. On 19th May, 1936, he suddenly developed signs suggestive of a ruptured duodenal ulcer. These signs subsided with 24 hours, and the abdomen became soft. However, the pains persisted, and on 25th May, 1936, laparotomy was performed. At operation, a small perforation was discovered in the first portion of the duodenum. This was sealed over, and a posterior gastro-enterostomy was performed. The patient developed signs of broncho-pneumonia on the third post operative day and expired on 29th May, 1936.

Diagnosis.—Clinical diagnosis was : thrombosis of left middle cerebral artery, ruptured duodenal ulcer and bronchopneumonia. Anatomic diagnosis was : thrombosis of left middle cerebral artery, duodenal ulcer with perforation and peritonitis, gastro-jejunostomy and bronchopneumonia.

Autopsy Observation on the Brain.—There was a large subarachnoid collection of fluid in the left temporal region, which escaped when the brain was removed. The brain weighed 1,200 grm. The vessels at the base showed moderate arteriosclerotic changes. The left hemisphere was smaller than the right, and along the line of the left Sylvian fissure there was a deep excavation (Fig. 1) with destruction of the entire superior temporal gyrus and Island of Reil, and the lowermost portions of the precentral, postcentral, supramarginal, and angular gyri. Broca's area, and the middle temporal and superior parietal convolutions were not involved. The brain was cut coronally (Figs. 2 and 3). In sections through the third ventricle, the area of softening was found to extend deeply to involve the claustrum and capsula externa, ceasing at the border of the putamen. The temporal horn of the left lateral ventricle was slightly dilated. In sections through the substantia nigra and splenium of the corpus callosum, part of the white matter of the centrum ovale was also destroyed. The area of destruction extended posteriorly to the end of the angular gyrus. There was no other lesion and no special atrophy of the brain cortex.

Summary and Discussion

In summary, here was a man, who following a cerebral insult, showed the following picture :—Although his general intelligence was not bad, there was a marked reduction in his spontaneity. His entire personality was narrowed. He was interested only in his own needs. His contact with the outer world consisted mainly in trying to defend himself against the disturbances which arose from it. He was friendly and co-operative in all relationships which he thought might help him, and was therefore very co-operative in all investigations. He was able to speak five languages. His general knowledge appeared to be little disturbed. His behaviour was, in the main, adequate ; the striking feature of it, was that he always reacted in a very concrete manner. In any situation, however, which required a " capacity for abstract attitude " (Gelb and Goldstein, 1924) he was completely unable to function adequately.

Perhaps the most striking symptom which the patient exhibited was his defect in speech. Within certain limitations, he was able to speak words and even sentences without paraphasia or dysarthria ; nor did he show any gross defect in understanding. There was relatively little disturbance in either the receptive or expressive aspects of his speech ; such defects in speaking and understanding as he showed, were not caused by any disturbance of the sensory or motor functions themselves, but by a deficiency in other functions, which we shall discuss.

Compared to this relative retention of his capacity for speech and understanding, it was amazing that the patient was totally lacking in the ability for repeating—either letters, words, or sentences. Inasmuch as his understanding was relatively unimpaired, this inability could not be attributed to a difficulty in hearing. Since there was no disability in motor speech, that could also be excluded as a cause. As we have mentioned, he could not repeat to command a word that he had just used spontaneously. Thus we cannot but assume that we were dealing with a disturbance of a special capacity for language repetition.

There has been a good deal of discussion about the psycho-physiological character of repetition, and of the anatomical basis for this capacity, a discussion which we cannot report here. We would refer the interested reader to the explanations of this phenomenon given by Goldstein (1927). Here we can mention only a few of the factors involved which are important for understanding the present case.

Repeating (nachsprechen) has generally been considered a very simple phenomenon. Thus Wernicke conceived of repetition of one's words as a simple overflowing excitation from the sensory to the motor part of the " speech " cortex in the form of a simple reflex arc and believed it to be based on the function of direct fibres connecting the acoustic speech centre in the temporal lobe (especially the fasciculus arcuatus). However, further investigations disclosed that this assumption does not correspond to analysis of the psychic phenomena, and that it does not agree with the anatomical findings in patients with lesions in this region. We know of cases in which these long association fibres have been destroyed, and the patient was able to repeat (Goldstein, 1915).

Repetition is not a simple reaction of a motor apparatus to a sensory stimulation. In repeating, we must be able to perceive the complicated sound of the spoken word and to imitate it more or less voluntarily by means of complicated movements. This leads to the assumption that a simple reflex arc could not be the basis of this function, but that it is dependent upon a more complex association system. This assumption is supported by the anatomical facts. Goldstein (1915) suggested many years ago that repetition is dependent upon the cortical apparatus of the Island of Reil, or to put it more accurately, greater or lesser destruction of this cortex results in more or less impairment in the function of repetition. This is strikingly borne out by the present case in which the total lack of the capacity for repetition can be correlated with the post-mortem finding of complete destruction of the Island of Reil. This parallelism has also been described by several other writers (Pick, 1898, Voisin, 1867).

In the light of this explanation, the peculiarity which our patient exhibited in his attempts at repetition, becomes understandable. As we have pointed out, in his attempts to repeat the given word, he would at times utter words which bore a definite relationship to it—e.g. " Himmel " (Heaven) for " God " ; " family " for " children " ; " glass " for " window," etc. Similar observations have been mentioned several times in the literature : Heilbronner (1910), Kleist (1931), Henneberg (1918), Goldstein (1906). Goldstein assumed that this behaviour is characteristic of a lesion of the Island of Reil, which makes impossible a real repetition, but which does not hinder the patient from understanding the general significance of the given word sufficiently to utter words which belong to the same " sphere."

Such a phenomenon occurs even in experience with normal individuals. We know that to grasp the general relationship or " sphere " of a heard word is an easier performance than the correct perception of the individual word. We often find ourselves in a similar situation if we are confronted with rare or foreign words. We understand in a vague way what the words relate to, i.e. in what sphere they belong, but we are not able to understand the sense of the individual words or to repeat them correctly. This happens particularly when the sphere of the word-stimulus corresponds to the situation in which we find ourselves.

The understanding of our patient was undoubtedly mainly of that type. Very often he failed to understand single words, particularly when they referred to spheres apart from the situation he was in. On the other hand, he understood relatively well sentences which belonged to the concrete situation in which he found himself. Hence strictly speaking we should modify our statement that the patient's capacity for understanding speech was relatively intact, by pointing out that although this was true in certain situations, the function of understanding speech was not really normal, but belonged to this special type of " sphere " understanding which we have just described. It is quite possible that this type of understanding is served by the right hemisphere in right-handed individuals (*vide infra*).

The second striking symptom which our patient exhibited, the inability to use name-words, can also be understood by the large defect in the Island of

Reil and the adjacent gyri in the temporal and parietal lobes, since, as we know, the lesions in so-called "amnesic aphasia," with which we are dealing here, show a predilection for this part of the brain (for a detailed discussion of the localization of the lesion in amnesic aphasia (see Goldstein, K. 1927).

The localization of the lesion in the left hemisphere agrees with the fact that the patient was a right-handed individual. However, a careful review of the entire clinical picture reveals some difficulties which the above explanation does not clarify. First, how was it possible that the patient heard and understood words and even sentences relatively well, if the temporal lobe of the left side was involved to such a degree by the lesion ? Not only was the so-called Wernicke relation in the first temporal convolution destroyed but also the general auditory centre of the left temporal lobe (the so-called Heschl's convolution). This defect forces us to assume that the patient's understanding of words must have been maintained by the corresponding part of the temporal lobe in the right hemisphere. However, should not the necessity of making this assumption lead us to doubt that the patient was a right-handed individual ? No. The patient's statements, and the observation of his predominant use of the right hand, made it more than probable that in essential performances he was right-handed. Furthermore, were he left-handed, it would be inconceivable that a left-sided brain lesion could produce such a severe incapacity for repetition and word-finding. Since this incapacity must be related to the left-sided lesion, it leaves no doubt as to the predominance of the left-hemisphere for the concerned speech function. Thus we have no choice but to assume that in our patient, in spite of the predominance of the left hemisphere, the integrity of the right hemisphere was able to guarantee understanding of speech, at least to a certain degree.

This would not contradict other experiences. We know from other cases that a gross defect in the capacity for understanding speech usually occurs only if—in addition to a lesion in the left temporal lobe—the pathways which connect the right temporal lobe with the left hemisphere are also damaged.

However, there is still another difficulty. Usually in cases of destruction of the Wernicke centre, and according to Goldstein, of the Insula Reili also, we find paraphasia. But our patient had no paraphasia ! One might assume that his good motor speech was due to the undamaged 3rd frontal convolution, were it not for the fact that usually, even when this convolution is intact, destruction of Wernicke's area or the Insula Reili still results in paraphasia. On the other hand, were we to assume that the absence of paraphasia was due to the function of the intact speech area in the right hemisphere, we would then have to ask, why was not the right hemisphere able also to guarantee repetition and word-finding ? Thus this latter assumption is difficult to maintain, and we would prefer to explain the absence of paraphasia in this case as due to the functioning of the motor speech area of the left hemisphere, perhaps in co-operation with the corresponding convolution in the right hemisphere. But does not this contradict the usual concept that correct word-speech is dependent on the function of the Insula Reili and the temporal lobe ? Not necessarily. Not infrequently, even in cases with lesions in these areas, some words and

sentences may be spoken without paraphasia—namely, such utterances which the patient has been accustomed to make without deliberation, which are delivered as mere motor automatisms. How much speech can be expressed in this way by an individual depends on his capacity for automatic motor speech. There are great individual differences. Owing to this varying capacity, a defect in other speech performances can be masked to a greater or lesser degree. Gelb and Goldstein (1924) have pointed out how we can be deceived regarding speech function in a patient with amnesic aphasia by the patient's use of his motor speech automatisms. The same mechanism can operate in a patient with paraphasia produced by a lesion of the Insula Reili or the temporal lobe. If the patient speaks little, and if his speech is largely restricted to the same well-known words and sentences, particularly if he possesses many such—then his paraphasia might not be discovered. There is some justification for assuming that this was the case in our patient. Although he spoke fairly well, he generally did not attempt to say much and usually uttered the same phrases and words. Although a simple man, he spoke five languages, and it is probable that being a simple man, he had especially well developed his motor speech automatisms in all these languages. It must be emphasized, however, that despite his knowledge of five languages, he could not find or repeat words to command in any of them.

To summarize our hypothesis, then, we may say :—We believe that the lack of the capacity for repetition and word-finding, was caused by the lesion of the Insula Reili and adjacent convolutions in the temporal and parietal lobes of the left hemisphere—corresponding to the patient's right-handedness ; his capacity for understanding speech was probably guaranteed by the right hemisphere ; his capacity for speaking without paraphasia, by the 3rd frontal convolution of the left hemisphere, perhaps in connection with the corresponding convolution of the right hemisphere.

There still remains, however, one very amazing finding in our patient which requires clarification. It is very unusual to find the capacity for repetition and word-finding disturbed selectively to as marked a degree as he exhibited. This fact demands a special explanation. We believe that the unusual extent of this disturbance in our patient took origin not only from the causes already mentioned but also from the particular change of personality which he exhibited. This change of personality has been described by Gelb and Goldstein (1924) as characteristic of patients with amnesic aphasia. According to these authors, the difficulty of finding words for naming, is only one expression of a change of the total personality. These patients have lost the " categorical " attitude and are reduced to a concrete level of behaviour. To them the normal attitude from which we name objects is entirely strange. Nominal words do not even occur to them. This is shown by the fact that our patient was able to use words in spontaneous or conversational speech which he could not utilize when asked to name an object. There was no doubt that he recognized objects. He could demonstrate how they were used, and occasionally, in explaining their relationship he would use the desired words, although he could never repeat them to demand or name the objects when they were presented to him.

In all these phenomena the patient's behaviour was similar to that of other amnesic aphasics. Both in his routine living as well as in special tests he revealed quite clearly the concreteness of behaviour which is so characteristic of this class of patients, differing from them only in the remarkable degree to which this concreteness was developed. One of us (K. G.) who has had the opportunity of examining many cases of amnesic aphasia, has never previously seen this phenomenon so pronounced in any of them.

Conclusion

An unusual case of amnesic aphasia is described clinico-pathologically. The receptive and expressive functions of speech were relatively only mildly disturbed. There was a striking impairment, however, in the naming of objects and the capacity for repetition. Added to this, there was a striking change in personality with loss of the capacity for abstract conception.

An attempt is made to explain the clinical picture on the basis of the anatomical findings. We are aware of the complexity of this endeavour, and although not entirely satisfied with our explanations feel that what we have suggested constitutes the most acceptable hypothesis in the light of available data.

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K. G. expresses his appreciation to the Rockefeller Foundation for special grants aiding this study.
The authors express their appreciation to Dr. Charles Davison for the neuropathological material used in this study.

Protocols

(1) The following protocol reveals the extent of the patient's vocabulary, his ability to make himself understood despite grammatical difficulties, and his comprehension of simple questions, particularly when they refer to his immediate situation.

The patient is co-operative, glad to see the examiner, and quite loquacious. He prefers a mixture of German and Yiddish, sometimes interspersed with English expressions. At times he is rather hard to understand. Paraphasia or dysarthria were not observed. His facial expression is vivid and adequate. He understands simple questions put to him in English or German. ("+" indicates a correct response)

(Your name ?) +
(Touch your ear !) +
(Where, here ?) +
(Who am I ?) (smiled, because question seems so simple). +
(Touch your eye), repeats several times " Auge, Auge." +
(Touch your ear) Idem. +
(Touch left ear with left hand.) +
(Touch right ear with left hand.) Perplexed, touches left ear, looks at examiner, cannot succeed.
(Touch right eye with left hand) Idem. He is not able to do tests with three items, as for instance touch with left hand first left ear then left eye. Asked what he has to complain about (a mixture of German and Yiddish) " Ich kann Sie kaum es sprechen aus—Ich habe ganz viel geleren—mein Kind sing gelernen—mein Frau ist da in Behandlung—die Kinder sind hier—ich kann bleiben. Die Leute so schmutzig—

die Finger—ich komme herein hier—sie machen so schmutzig—ich lieb nicht die Leute. Mein Sohn verheiratet, a ganz feine Mann—ich moechte that is mein Sohn—seine Frau—mein Tochter—sie ist in high school—English—ich moeg so gerne—I can speak French, too, parfaitement. I was in that position there—in 100 Street—mein wife—my children, one child was home. I got nice home—I come home—my wife—you eat something—it come 8 o'clock " Gustaf, you feel goot ? "—I feel goot. Half an hour later what happens—mein Gustaf—he's dead. I had twenty professor—many—my children all bring—he dead—cannot sprechen—Ich habe garnicht gewissen—wass—ich weisse garnicht was (what is your son doing ?). Was von mein Sohne ? was tut er ? what is he doing—ja—he was there 20 years. Er war sehr gute Mann. He has a business. (What is the doctor doing ?) He writes. (What with ?) Everything what you wish.

(Has your son such things—bottle of glue ?)—He's a printer—yes—he's got everything, he's got a nice business—he's got such things—but he has not use for dose things. Years ago—he used to make dem—but not now (pointed to book)—he does this things—he writes this things with a machine—a big machine—here, here and here—he's the boss—ya (what do other men do ?)—I know (shakes head) (printer ?)—yes—he's working over—others working for him getting $25, $40 a week. He does every work. He does difference work—I don't remember—I used to remember—I asked him how's business—" oh great, papa "—heute you erregnerich ?—yes it looks like rain to-day—but it's cold—the sun did not shine (does the sun shine ?)—yes, no, but I can't say—I know rain, rain it is nice warmer, warmer, colder (sky ?)—it don't look like rain. (Say the same words as I say) :

rain—Mein Herr.

rain—rain, it's raining, it's raining.

sky—I am sorry, I wish I could say every word. God, God is always there—God—I know—I understand (but the sky—it's raining)—not now—not raining no more. Gut gestern raining all night.

holidays—kosher—yo. . . yontiff, I know, I understand what is yontiff, to-morrow, Sunday, Monday, Monday it will be finished, Pesach, Easter.

(2) Manikin Test (Pintner and Paterson, 1931) : This little test, although relatively simple, involves the capacity of the patient to form a " Gestalt," i.e. to abstract a conception from a group of apparently dissociated objects. In spite of its simplicity we see that this previously highly intelligent individual had difficulties with it. Although he finally solved it more or less correctly, he had to proceed in trial and error fashion.

First he recognizes object by legs, head, and then seems to recognize readily that it is a man. Puts two legs together, using words " Fuesse, shoes." Puts two arms together, and points to his own arms. Patient then puts legs to trunk, but in wrong order—he just pushed them up without looking at the form outlined. He sees error, reverses legs, and inserts correctly. Puts left arm in right socket (it being nearest), sees mistake, corrects it. Puts other arm, then head in place. Arms put close to sides—not partially abducted. Patient quite joyous upon completion. Time : 3.15.

(3) Feature Profile Test (Pintner and Paterson, 1931) : This test is somewhat more complicated than the Manikin Test in that it involves the handling of two factors by the subject—one the grasping of the outer form of the test pieces, and the other, the grasping of lines on the test pieces which when put together properly form the eye, ear, nose, etc. The fusing of two such factors involves what we speak of as the capacity for abstract conception. As the test shows, the patient was lacking in this ability.

Cannot say what it is by its outline form. Uses trial and error to fit forms of profile. When he fits correctly " That's right." He knows when he is right or wrong. Completes profile, then " oh, my God, a whole Kopf." First looks along outside of figure in order to fit earpieces. Must then be shown hole in centre. Starts with trial and error inside—no success—then tries to put ear together on outside. He uses the lines on the blocks—knows when he is wrong. Puts two pieces correctly, but cannot fit other two to them. He refuses to accept his own results because he knows that they are not correct. " No, sir, it's very hard, very hard." (After about 6½ minutes work—" shall I show you how? ") Patient asked to repeat, but no success. Illustrated once more—then asked what it might be. Patient cannot say. Picks up all pieces together—" maybe if I put it inside, I could tell you." Put ear inside, picking all four pieces together and thus putting them in place, smiles, points to his own ear and says " nose."

(4) Colour Sorting Test. This test reveals more clearly than any of the other tests the particular nature of the patient's intellectual deficiency. It will be noted that he seemed to be completely unable to grasp the idea of " colour " as an abstract conception. He was able to think only of particular shades. Thus, he could not see the categorical connection between a light green and a dark green. To him they were different colours, and under no circumstances could he be induced to realize that they belonged in the same general grouping. When he used the words " green " or " red," it became clear that he was not using the terms in their generic sense, but was referring only to the particular shade of green or red that he had under observation at the moment. Similarly, although he at times would match bright shades of different colours to a given bright shade of red, he was nevertheless totally unable to grasp the *idea* of " brightness " as an abstract concept, and could not pick out bright shades of different colours on demand.

The patient is asked to pick out from a heap of assorted coloured yarns all those strands which are similar in colour to a given sample.

(*a*) Medium green.—He picks up a medium green. " That is a heller (brighter) green. Dies heir green, das is schoener green." He picks up a very light green. " Das heller (brighter)." He does not consider it a match and puts it aside. He picks up a dark red. Looks at the green sample, and says " No." He picks up a dark blue and a dark purple. Looks at the sample. " No, das anderes (different)." Picks up a dark green, matches it with the sample, then replaces it, apparently dissatisfied with the match. Picks up a dark purple. " No, das nicht dasselbe (not the same)." Picks up a light shade of green. " Das is greener, die mehr." Replaces it in the original heap. Picks up a very similar green to the given sample—an almost perfect match. " Ja, ja, dasselbe ! " Takes other greens and attempts to match them, but returns them to the heap. Feels satisfied and joyous only when he is able to match the sample with others of almost identical shade.

(*b*) Goes through the same procedure with a given red.

(*c*) An attempt is made to demonstrate to the patient what is desired of him by putting a series of different reds in one heap, and a series of different greens in another. However, the patient was apparently unable to grasp the principle involved, and refused to admit correctness of the division. He showed satisfaction only when identical or near-identical shades were matched.

(*d*) Given a very light blue—matches with two light shades, but is dissatisfied. " No, no, auch nicht." " Beinahe, aber nicht dasselbe (almost, but not the same)." He picks other skeins of comparable brightness—very light blue, very light purple,

very light grey, very light grey, very light grey, very light grey, very light green, very light brown, very light blue, very light yellow. However, when asked shortly afterwards to select light shades of different colours, he is unable to do so.

(*e*) He is shown a light blue, a dark blue, and a dark red, and is told that the light blue and dark blue match better than the dark blue and dark red. He shook his head, saying, " No, das blue, das is ganz andere. No, das blue, everything, nicht das, nicht das."

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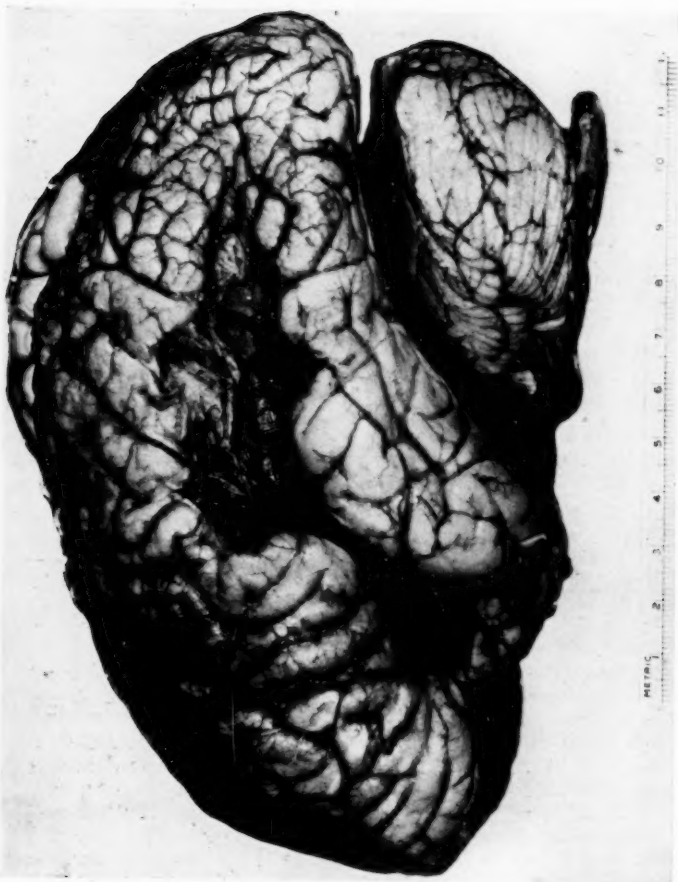

Fig. 1.—Left lateral aspect of brain. Partial thrombosis of left middle cerebral artery, with destruction of the insular and superior temporal convolutions, and the lowermost portions of the precentral, postcentral, supramarginal and angular convolutions. Note the complete sparing of Broca's area.

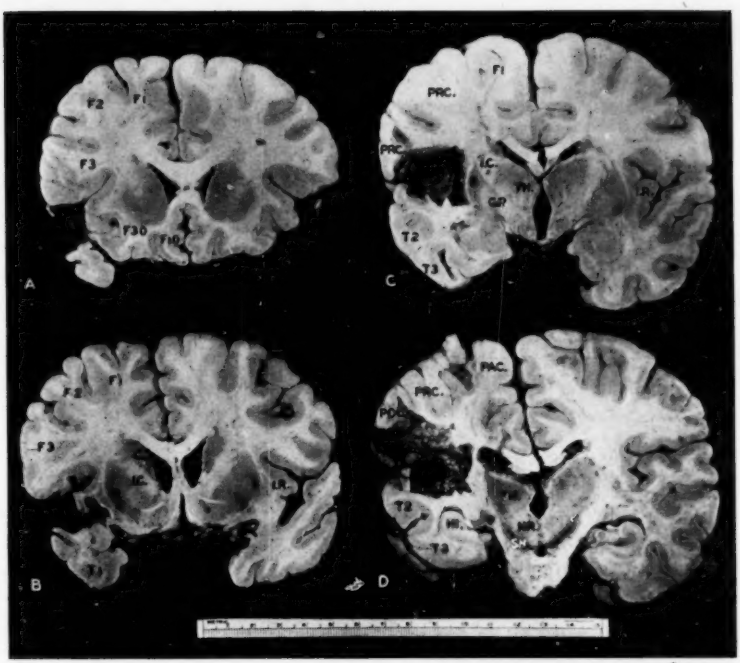

Fig. 2.—Coronal sections through the genu of the corpus callosum, the striatum, the third ventricle, and the substantia nigra. F1, F2, F3—frontal convolutions ; F10, F30—orbital convolutions ; C—caudate ; I.C.—internal capsula ; I.R.—Island of Reil ; P.—putamen ; G.P.—globus pallidus ; T1, T2, T3—temporal convolutions ; TH.—thalmus ; PRC.—precentral ; POC.—postcentral ; PAC.—paracentral ; HI.—hippocampus ; N.R.—nucleus ruber ; S.N.—substantia nigra. Note sparing of Broca's area (F3).

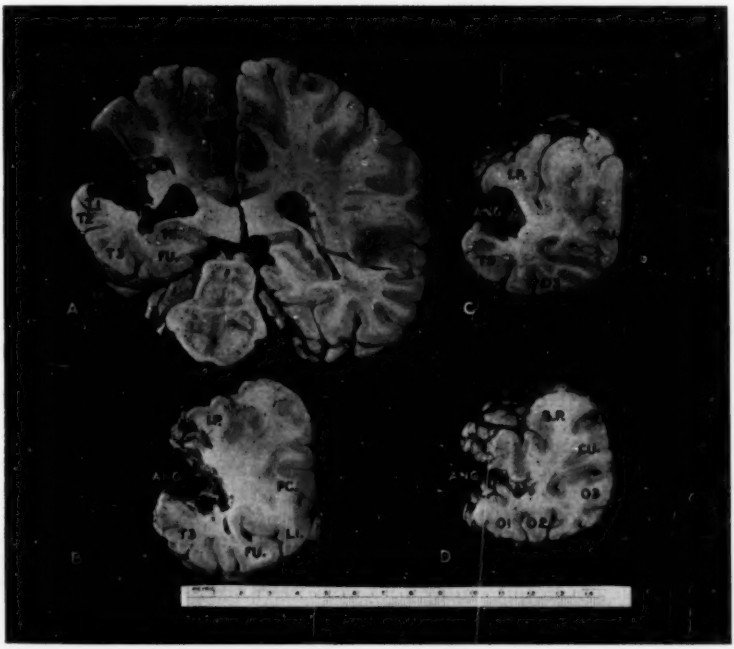

Fig. 3.—Coronal sections through the splenium of the corpus callosum, and the left occipital lobe. S.P.—sup. parietal ; I.P. inf. parietal ; H.I.—hippocampus ; FU.—fusiform ; T1, T2, T3—temporal convolutions ; PC.—precuneous ; L.I.—lingual ;

THALAMIC HYPERTROPHY OR GLIOMATOSIS OF THE OPTIC THALAMUS

BY

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(RECEIVED 29TH JULY, 1938)

Introduction

IT is well recognized that in the optic nerves and brain stem tumours of the glioma group frequently give rise to a general enlargement of the area involved, rather than a localized tumour formation. In such cases the new growth is diffuse and infiltrating, and there is considerable variation in the size, shape, and type of the tumour cells, so that classification of these tumours on an embryological basis has proved difficult. Similar types of growth may involve the optic thalamus. Here, however, they have been less frequently studied, although diffuse glioma of the brain stem generally extends to some degree into the optic thalamus. It is possible that cases in which the thalamus is predominantly involved are not common, and it is therefore proposed in this paper to describe three such cases, and to discuss their pathology and relationship to gliomas in general. The appropriate literature will be referred to after the general discussion.

Case 1

CLINICAL HISTORY.—P.S., a girl aged seven, was admitted to the Hospital for Nervous Diseases, Maida Vale, on the 25th October, 1935, under Dr. Feiling. She died on the 19th November, 1935.

The family history was negative. The patient was born with café-au-lait spots on her hip and back. She went to school at five years of age, but made no progress, and was clearly not as intelligent as her brothers and sisters. She was well up to ten months before her death, when she became quiet, played less with other children, and began to lose weight. She also began to have vacant turns, and four months later she complained of headaches and loss of vision in the left eye. The headaches increased in severity, and after admission to hospital they were very continuous and frequently associated with vomiting.

On examination she was very thin and wasted, drowsy and inco-operative. The left eye was blind, and the optic disc showed primary optic atrophy. Vision in the right eye appeared to be normal ; the visual field was full to rough tests and the optic disc was normal. The right pupil reacted well to light, but the left only very slightly. There was slight weakness of the left sixth nerve. The musculature generally was thin and wasted, but no alteration in motor power, reflexes, or sensation was observed.

X-ray of the skull showed slight downward displacement of the anterior clinoid processes, especially the left, which was also partially eroded. At operation a large hypothalamic tumour was found, the greater part of which was removed, but the patient died the next day.

POST-MORTEM EXAMINATION.—On removal of the brain the hypothalamic region was found hollowed out by the tumour and the pituitary region of the skull flattened and thinned. The floor of the third ventricle forwards from the corpora mammillaria was destroyed and there was dilatation of the antero-inferior part of the third ventricle. Vertical section of the brain revealed that the thalami were paler and firmer than normal and slightly enlarged throughout their whole extent, but no other abnormality was observable with the naked eye (Fig. 1).

MICROSCOPICAL DESCRIPTION.—*The Hypothalamic Tumour.*—This consisted of round, oval, and elongated nuclei with well-defined nuclear membrane and a granular

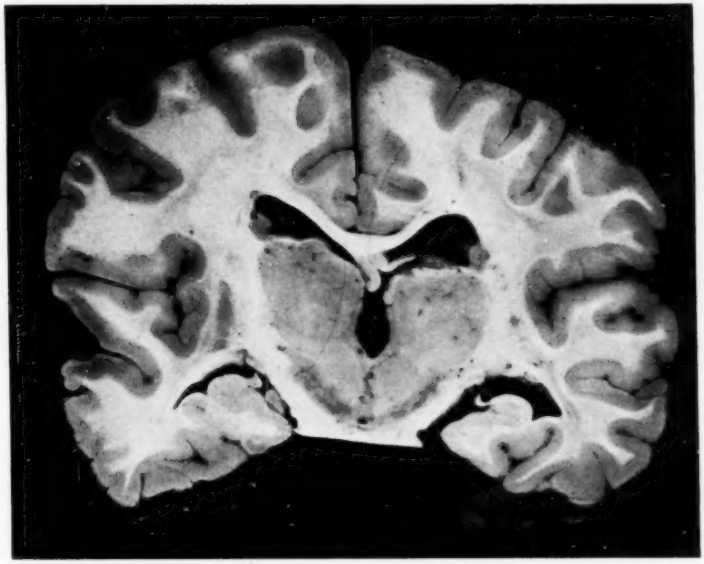


Fig. 1.—Case 1 : Vertical section of the brain, showing the slight bilateral enlargement of the thalamus.

chromatin network lying in a light fibrillar stroma (Fig. 2). No cell body was seen with ordinary nuclear staining. In parts the microscopic field was filled with loosely arranged nuclei varying very much in size and shape, while in other parts fibrillar bundles of elongated cells were found. There was dense cellular condensation along some blood vessels, and the irregular fibrous tissue coat of these vessels was infiltrated with tumour cells. Coarse, thick neuroglial fibres were everywhere present in the tumour. These could often be seen arising from bipolar or irregular shaped cells in Mallory or Victoria blue preparations, but there were also numerous rounded cells with no processes. These were especially numerous in the irregular masses around the blood vessels. The tumour may be designated a polar spongioblastoma, although this does not accurately describe its histogenesis. It is clearly very similar to the gliomas occurring in relation to the optic nerve, and it may possibly have arisen from the left nerve, as the optic chiasma showed a slight new formation of irregular shaped neuro-

glial cells. It was localized to the hypothalamic region, and did not invade the optic thalamus or adjacent structures.

The Optic Thalamus.—On microscopical examination the thalamic hypertrophy was found to be due to a diffuse new growth of neuroglial cells, which was nowhere very intense and had not produced any definite changes in the essential nervous elements (Fig. 3). No cell body was seen with ordinary nuclear staining, but Hortega's silver carbonate method for astrocytes revealed that the cells varied in size, shape, and type from immature spongioblasts to enlarged and irregularly shaped astrocytes. In the spongioblasts the nucleus was for the most part small and round and heavily impregnated, and the cell body generally small, round, or oval with a coarse granular appearance and no very definite cell membrane. The cell body often tailed off into a single process, but frequently no process could be stained. Bipolar cells were rarely seen. In some cells with round nuclei the cell body was larger, and several rudimentary processes could be made out, although the general staining of the cell body was similar to that in the small unipolar spongioblasts. The irregular-shaped nuclei showed little cell body, but faint processes could be made out opposite the angulation

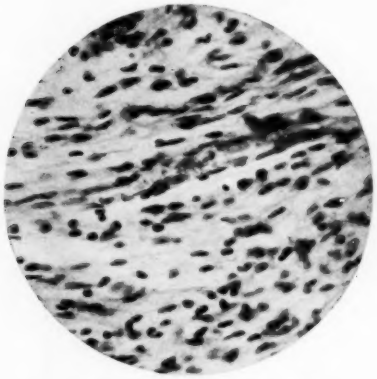


Fig. 2.—Case 1 : Structure of the hypothalamic tumour. (Hæmatoxylin and eosin.)

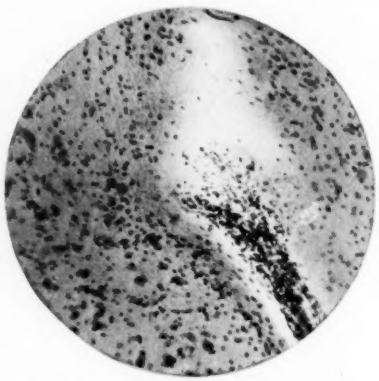


Fig. 3.—Case 1 : The diffuse cellular overgrowth in the thalamus. (Iron hæmatoxylin and van Gieson.)

of the nuclei. Such cells were probably transition stages between the spongioblasts and the mature astrocytes. The latter varied very much in size ; the nucleus was granular and lighter stained than in the spongioblasts, and the cell body was clear with a definite cell membrane and sharp though faintly stained cell processes.

The new-formed cells were scattered fairly evenly throughout the thalamus, and they also extended into the upper part of the midbrain. Frequently little clumps of three or more cells were found, especially around nerve cells. There was also some cellular accumulation around some blood vessels and underneath the superior and inferior surface of the thalamus and round the margin of the brain stem. This was associated with dense, fine gliosis which also extended irregularly throughout the thalamus and upper part of the midbrain as a loose network varying from point to point. That round the blood vessels consisted of closely packed piloid bundles of fibres running in the long axis of the vessel. This glial condensation displaced the myelinated fibres in a regular manner from the immediate proximity of the larger vessels. The increased marginal gliosis around the midbrain extended down the brain stem to the upper part of the spinal cord. It spread inwards irregularly in different regions and throughout the brain stem elongated and irregularly shaped neuroglial cells were everywhere present. There appeared also some increase of cells

in the internal capsule, while in the lenticular nucleus and island of Reil the neuroglial nuclei were very irregular in size, shape, and form although there was no definite cellular increase. The actual limits of the cellular overgrowth in the thalamus were therefore difficult to define.

The cerebral cortex was not involved in the new growth, but in different areas there was increased marginal gliosis, which in some fissures was adherent to the walls of the blood vessels. In these sites recent hæmorrhage had occurred around the blood vessels and between them and the cortex.

Changes in the Essential Nervous Structures.—Myelin preparations showed no gross demyelinization in the thalamus or brain stem, and the internal capsule was darkly stained. Also in these areas the nerve cells were normal in appearance, and there was no definite alteration in their number or arrangement. In the giant celled precentral area of the cortex, however, many of the large pyramidal cells were very irregular in shape, and the protoplasm stained darkly and diffusely, showing little differentiation of Nissl granules. In some cases excessive branching of the dendrites close to the cell body occurred, and others were abnormally placed, the apical dendrite pointing towards the white matter, while the nucleus was also displaced to one or other side. These changes were present in numerous sections from both hemispheres. Their pathological significance is doubtful, but they may possibly indicate some slight developmental abnormality in regard to the cells. A detailed study, however, of the cerebral architectonics was not made.

Summary and Discussion of the Case

The case was characterized clinically by a slight degree of mental deficiency, skin pigmentation as in Von Recklinghausen's disease, and for ten months before her death the signs and symptoms of a hypothalamic tumour. Pathologically, as well as this tumour there was present a symmetrical hypertrophy of the thalamus. This resulted from a diffuse overgrowth of spongioblastic and astrocytic cells very variable in size, shape, and type throughout the thalamus, and extending also into the upper part of the midbrain. This new growth of cells was clearly of blastomatous origin, but it did not admit of classification as a single type of tumour formation. It is unlikely that a tumour could arise in one place and spread through the thalamus in such a way as to give rise to dense perivascular gliosis and cellular accumulations round the nerve cells. The varied form and differentiation of the cells would also require two or more classifications of the type of growth. The cellular proliferation appears to have developed locally over a wide area, and may therefore be designated a gliomatosis of the optic thalamus. The presence of other abnormalities, some clearly developmental, such as the café-au-lait patches on the skin, the marginal gliosis in the cortex and the brain stem, and the hypothalamic tumour suggest the possibility that the growth may be congenitally predetermined. As a developmental abnormality neuroglial cells capable of giving rise to it may be present over a wide area. They may be mature or undifferentiated, but as differentiation of the multiplying cells seems a feature of the growth, the latter is more probable. The factors determining the origin and rapidity of the cellular proliferation are entirely obscure, which is also the case with regard to blastomatous malformations in general.

Case 2

For this case I am indebted to Dr. Denny Brown and Dr. Greenfield, and the notes are from the routine clinical and pathological records of the National Hospital, Queen Square.

CLINICAL HISTORY.—A.B., a man aged 60 years, was admitted to the National Hospital on 8th March, 1937, under Dr. Denny Brown. He died on 31st March, 1937.

He had one younger brother, who was subject to fits, and his first wife, who came of an epileptic family, had two children, one of whom was epileptic.

Apart from a severe blow on the chin at the age of forty, the patient suffered no illness and was well up to six months before his admission to hospital, when he began to complain of headaches, drowsiness, and failure of memory. The onset of these symptoms was gradual, and they slowly became worse. The headaches were chiefly vertical and came in severe attacks of short duration. He was continually drowsy, and he tended to fall asleep several times in the day. The failure of memory was especially for recent events, and he would forget the day of the week and even which bedroom he occupied. Before admission to hospital he also complained of giddiness and general unsteadiness in walking.

On examination he was drowsy, but co-operative. His speech was slow, but otherwise normal. He was normally orientated in time and place. There was no papillœdema nor other abnormal sign in the cranial nerves. The motor system reflexes and sensation were all normal, but his gait was slow and slightly unsteady. The cerebrospinal fluid was under a pressure of 230 mm. of water and was normal except that the total protein was 90 mgms. per 100 c.c. and the globulin tests were positive. Ventriculography by Mr. Jackson showed defective filling of the body of the right lateral ventricle and deviation of the ventricular system to the left. The patient gradually became worse and died, operative interference not being considered advisable.

POST-MORTEM EXAMINATION.—The brain weighed 1,700 grammes. The medulla, pons, and right mammillary body appeared enlarged to the naked eye. Horizontal section revealed a uniform enlargement of the right optic thalamus, which bulged markedly into the third and right lateral ventricles (Fig. 4). The right thalamus was also paler and firmer than normal, except in the antero-medial part, which was softer than normal. The corpus striatum on the right side and the grey matter in the depths of the island of Reil were slightly paler than normal. The left hemisphere was normal in appearance, and the normal configuration of the brain was everywhere preserved.

MICROSCOPICAL EXAMINATION.—This revealed that the naked eye changes were produced by a widespread cellular overgrowth which was most severe in the right optic thalamus, but also extended throughout the brain stem and the basal ganglia and adjacent areas of the right cerebral cortex. The microscopical features of this new growth will be described in the optic thalamus, and then its general distribution and variations will be followed.

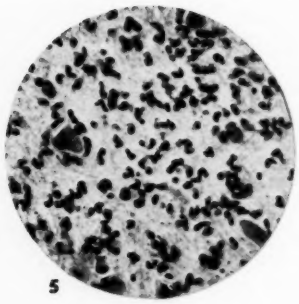
In the thalamus nuclear stains revealed a diffuse and fairly regular cellular infiltration throughout the whole organ, which was, however, most dense antero-medially. The nuclei closely resembled normal neuroglial nuclei in general structure, but they varied greatly in size and shape. There were round, smoothly elongated, polygonal shaped, and irregularly lobulated forms, and the size varied from that of oligodendroglial nuclei to that of nerve-cell nuclei (Fig. 5). The polymorphous forms sometimes showed fine chromatin threads connecting two or three lobules, and dumb-bell and horse-shoe shaped forms also occurred. With Hortega's silver carbonate method for astrocytes the cells were found to be astrocytes and spongioblasts with a great variation in the form of the cell body corresponding to the variation in nuclear shape (Figs. 6, 7, and 8). The astrocytic cells showed a lightly staining and well-defined

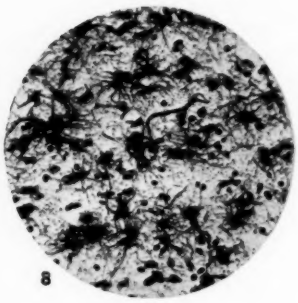
cell body and sharply outlined cell processes. Some were small, with hardly any cell body, and others very large, with coarse, thick processes which could be seen to extend long distances from the cell. Medium-sized forms were numerous ; many appeared elongated, others were triangular shaped, and some contained two nuclei. These cells formed only a part of the cellular overgrowth, and there were present numerous more immature cells. Some of these had a clearly outlined cell body, which was, however, faintly stained with no definite cell membrane and a few indefinite cell processes. In others, especially with very irregular shaped nuclei, only a little cell protoplasm but no processes could be stained, and in relation to some nuclei even this could not be made out. Some cells could, however, be labelled polar spongio-

Fig. 4.—Case 2 : Horizontal section of the brain, showing the diffuse enlargement and pallor of the right thalamus and also the pallor and increased depth of the cortex in the island of Reil.

blasts because the nucleus was round or elongated, and a long process, faintly stained, could be seen passing away from one pole of the cell. These were small, but similar cells in which the bodies and processes were large and thick, and stained similarly to the giant astrocytes, were also present (Fig. 7). The processes of these, and also those from astrocytic cells, were frequently attached to vessel walls. Bipolar spongioblasts were rarely seen. The different types of cells were evenly mixed throughout the tissues, but little clumps occurred around nerve cells and frequently one or two astrocytic cells were grouped with several more immature cells.

In the posterior part of the thalamus the growth was moderately severe, and many astrocytic cells with round cell body and numerous processes arising right round the cell body were present. Some of these lay close to nerve cells, and then their processes enclosed the nerve cell as in a basket (Fig. 6). The processes of these cells





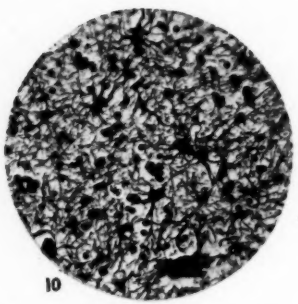


Fig. 5.—Case 2 : The varied size and shape of the nuclei of the cellular overgrowth in the thalamus. (Iron hæmatoxylin and van Gieson.)

Fig. 6.—Case 2 : The different cell types in the thalamus, and the processes of the blastomatous cells enclosing the nerve cells. (Hortega's silver carbonate method for astrocytes.)

Fig. 7.—Case 2 : Another field showing predominantly large unipolar cells. (Hortega's S.C.A.)

Fig. 8.—Case 2 : The diffuse glial overgrowth in the thalamus. (Anderson's Victoria blue.)

Fig. 9.—Case 2 : The cortex of the island of Reil showing the new-formed cells with no fibre production in the background ; to be contrasted with Fig. 10. (Hortega's S.C.A.)

Fig. 10.—Case 2 : The subcortical white matter of the island of Reil showing the fibrillar nature of the overgrowth. (Hortega's S.C.A.)

were well stained with Victoria blue, and a fine glial network of varying density was present (Fig. 8). There was also glial condensation round the vascular spaces. In this area of the thalamus there was little alteration in the essential nervous structures compared with the degree of new cell formation. Degenerating nerve cells were sometimes seen, but there was no great reduction in their number. Those remaining contained large accumulations of lipoid staining dark red with Scharlach R. In the softened area of the anterior part of the thalamus the cellular overgrowth was very dense, and more immature cell forms were present and the neuroglial fibre production was slight. There was also much greater destruction of the essential nerve structures, although numerous myelinated fibres and nerve cells were still present. Scharlach R preparations showed much dark red lipoid scattered throughout the area, while myelin stains showed that the slight general pallor of the whole thalamus was accentuated in this region.

General Distribution of the Cellular Overgrowth.—The internal capsule showed no demyelinization, and in this structure the cellular overgrowth was much less, and the nuclei were for the most part round or elongated in the direction parallel to the fibres. In the caudate and anterior part of the lenticular nucleus the density of the cell proliferation corresponded to that in the posterior part of the thalamus. There was, on the whole, less formation of fine glial fibres between the cells, except on the postero-medial part of the globus pallidus adjacent to the internal capsule. In the antero-inferior part of the globus pallidus there was a small oval area of complete demyelinization, and in this the cellular overgrowth was dense and the cells were astrocytic with swollen cell bodies similar to gemastete cells. There were other immature cells present in the focus which were not swollen. In the anterior commissure the cellular overgrowth was not severe, but it gave rise to a fine gliosis which tended to be arranged parallel to the direction of the fibres, and this contrasted strongly with the appearance in adjacent parts of the caudate and lenticular nucleus, where the round astrocytes with numerous processes did not seem to give rise to a great glial fibre formation throughout the tissues.

The new growth in the right hemisphere also involved the depths of the island of Reil, the antero-medial part of the temporal lobe, the anterior part of the corpus callosum and adjacent white matter, and the medial surface of the hemisphere.

In the island of Reil it was greater in the cortex than in the subjacent white matter, and was of such a degree that it led to gross destruction of nerve cells so that the cell layers were not recognizable ; also the residual nerve cells were filled with lipoid. The new-formed cells were, for the most part, mature astrocytes of medium size with sharply stained cell processes, but they did not give rise to a glial network in the background (Fig. 9). In the subjacent white matter, although the cellularity was much less, a glial network was present (Fig. 10). The involvement of the frontal lobe was most marked immediately underneath the ventricular surface, where a subependymal overgrowth of bipolar spongioblasts and round or oval cell forms was found. These cells extended considerable distances into the subjacent white matter and large condensations were present around numerous blood vessels. Small areas of the adjacent cortex were also involved and here a slight cellular overgrowth extended right through the cortex to the pia arachnoid.

In the left optic thalamus and basal ganglia there was no definite cellular overgrowth but the neuroglial nuclei were in general larger and very much more irregular in size than normal.

The new growth extended throughout the whole extent of the brain stem and involved also the commencement of the spinal cord. Weigert Pal preparations of the brain stem showed no pallor or tract degeneration. It was in general greater on the right side, and was similar to that found in the thalamus and basal ganglia. In the pons it was greater dorsally than ventrally and in the pontine nuclei more than in the fibre bundles. It was everywhere accompanied by a network of glial overgrowth which varied very much in density. There was also increased marginal gliosis throughout

the whole extent of the brain stem. The cerebellum did not show any definite abnormality, but in the region of the dentate nucleus there appeared to be much greater variation than normal in the size and shape of the neuroglial nuclei. It is recognized, however, that great variations have been described in the normal neuroglia in this region, so that the significance of this point is doubtful.

Summary and Discussion of the Case

The case was characterized clinically by a six months' history of headache, drowsiness, and failure of memory. Pathologically there was found a new growth of spongioblastic and astrocytic cells throughout wide areas of the central nervous system, predominantly affecting the right optic thalamus, but also the adjacent areas of the cerebral hemisphere and the brain stem. The overgrowth was superimposed upon the essential nervous elements, and had only led to severe alteration of these structures in the small area of greatest growth in the anterior part of the right thalamus. It was impossible to define clearly the limits of the growth, as slight changes extended widely from the main lesion, and the difficulty was to pronounce the neuroglia entirely normal in the uninvolved regions of the brain, as for example, in the dentate nucleus. With regard to the nature of the new growth, it seems impossible to classify it as a tumour formation which had arisen in some area and spread, either by fibre tracks or along vascular pathways or in some other manner widely throughout the nervous system. This would presuppose a remarkable ability for migration among normal tissues of individual tumour cells, and an ability to stop in special sites, as for example, around nerve cells and in the grey matter of the pons, which was more predominantly affected than the adjacent white matter. Moreover, the cells have not escaped entirely from the influence of the surrounding tissues, as is shown clearly by the different character of the cells in the grey and subcortical white matter of the island of Reil. Furthermore, differentiation of multiplying cells seems an essential feature of the cellular proliferation, because if such is not the case the regular arrangement throughout the affected area of cells in various stages of differentiation from spongioblasts to astrocytes is difficult to understand. For these reasons the pathological process has been considered a diffuse gliomatosis which has arisen *in situ* over a wide area, or having commenced in one area has affected adjacent areas by liberation of chemical substances or growth factors. On this basis the involvement of the temporal horns and the white and grey matter of the medial surface of the hemisphere is more easily understood. A developmental predisposition to the blastomatous change seems likely, although there is no direct evidence for this factor, apart from the abnormal variation in form of the neuroglial cells in parts of the uninvolved cortical areas. The origin of the growth, therefore, is probably from widespread abnormal neuroglial cells perhaps not fully differentiated, but the factors determining the late onset and rapidity of the growth of the proliferating cells are entirely obscure.

Case 3

CLINICAL HISTORY.—S.N., a married woman aged 46, was admitted to Maida Vale Hospital on 21st December, 1936, under Dr. Golla. She died on 1st January, 1937.

The family history of the patient was negative. She herself was well up to nine months before admission to hospital. At this time, following her mother's death, she seemed to lose interest in things, became forgetful, and began to complain of headaches. The headaches, which at first occurred once or twice a week and lasted two or three hours, became more frequent and more severe, and were associated with drowsiness and at times disorientation and confusion. These symptoms gradually progressed and she became listless and dreamy and unable to take care of herself.

ON EXAMINATION.—She was drowsy and inco-operative, and it was difficult to hold her attention. She understood simple commands, knew where she was, and recognized her friends. Her memory was vague for recent events and her speech was very slow. She was also incontinent of urine and fæces. There was no papillœdema and the cranial nerves were normal except that the pupil reaction to light was diminished in both eyes, especially the right. She lay in bed on her back with arms

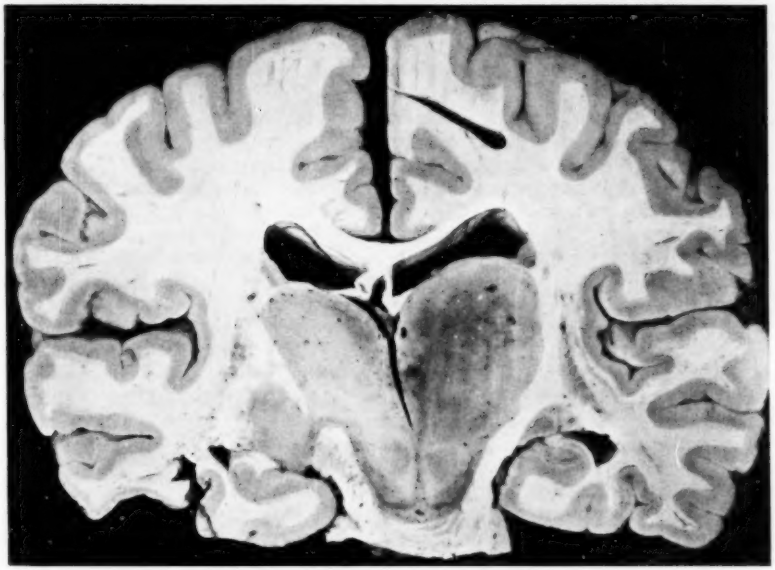


Fig. 11.—Case 3 : Vertical section of brain showing the enlargement of the optic thalami.

flexed and adducted and legs flexed. There was a generalized resistance to extension of the limbs. The rigidity seemed greater on the right side, and an irregular tremor was occasionally present in the right hand. No gross loss of power could be made out. Except that the left plantar was extensor and the left knee-jerk increased, the reflexes were normal. No definite sensory change was detected. The cerebrospinal fluid was normal, and the pressure was 175 mm. water. The patient gradually became weaker, more drowsy, and one week after admission lapsed into unconsciousness, with stertorous breathing, loss of reflexes, and died in half an hour.

POST-MORTEM EXAMINATION.—Apart from a slight cerebellar pressure cone, there was nothing to note on the external surface of the brain. Vertical section revealed diffuse enlargement and discoloration of the optic thalami, especially on the left side, narrowing of the third ventricle, and moderate dilatation of both lateral ventricles and a linear area of cavitation in the medial part of the left cerebral hemisphere (Fig. 11). The left thalamus was diffusely enlarged throughout its whole

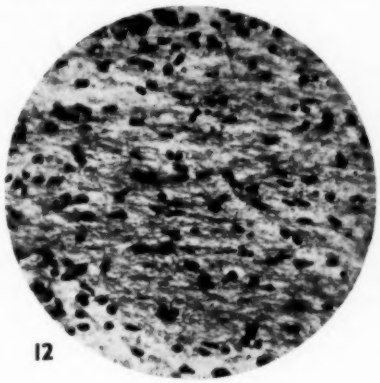
extent, curving the internal capsule outwards, pushing the flattened third ventricle across the midline, and narrowing the body of the left lateral ventricle. The consistency of the whole organ was softer than normal, especially in its centre, which was also hæmorrhagic. The hæmorrhagic zone covered practically the whole transverse section of the thalamus at its centre, but decreased in extent anteriorly and posteriorly. The right thalamus was only slightly enlarged posteriorly. It was slightly paler than normal, but its consistency was not greatly altered. There was also an area of pallor inferior and lateral to the right thalamus and underneath the lenticular nucleus. It involved the tail of the caudate nucleus, the outer part of the internal capsule, and extended in an antero-posterior direction the whole length of the thalamus. The cavitation in the left hemisphere extended about two inches in an antero-posterior direction, was bridged over by the arachnoid, and the adjacent cerebral fissures extended into it. In its depths there was a thin lining membrane of indefinite structure, but towards the medial aspect of the hemisphere this was absent and the surface was more irregular. There was no surrounding gliosis and it was considered most probably the result of some developmental defect, but its pathogenesis was not clear.

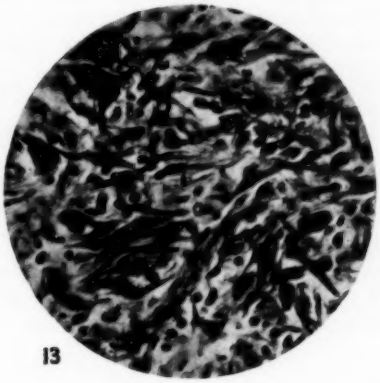
MICROSCOPICAL DESCRIPTION.—Microscopical examination revealed that the naked eye changes were produced by a diffuse new growth of neuroglial cells throughout both optic thalami. This varied in density and cell structure in different areas.

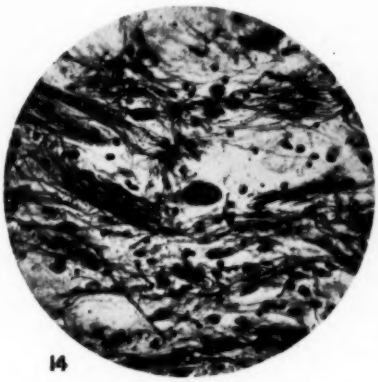
In the right optic thalamus the cellular overgrowth was of moderate intensity and composed of cells with round, oval, or irregular-shaped nuclei, with a granular chromatin network which varied very much in density. Their size in general resembled neuroglial nuclei, but many were larger and many smaller. This cellular proliferation extended throughout the whole thalamus, but was greater posteriorly and least marked anteriorly, where there was only a slight increase of neuroglial cells with irregular shaped nuclei. Hortega's silver carbonate method for astrocytes revealed that the cells were astrocytes and more immature neuroglial cells. The former were for the most part fairly large cells with a sharp but lightly stained cell body and well-defined processes. A few smaller astrocytes were present. Immature cells appeared more numerous than the astrocytes, and in many of these no cell body could be stained. Others showed a round or irregular cell body which was granular and ill-defined. Unipolar and bipolar spongioblasts were seen, but these were not numerous except in the condensation round the blood vessels, where bundles of bipolar and astrocytic cells associated with piloid masses of glial fibres were present. There was a general increase of neuroglial fibres throughout the thalamus (Fig. 12). This varied from point to point, and was always greatest around the blood vessels and in general towards the medial and inferior aspect of the organ. This new growth was superimposed upon the essential nervous elements of the thalamus, which had undergone little destruction compared with the intensity of the new cell formation. Some degenerating nerve cells, however, were seen, and those preserved showed large accumulations of fat in the cell body with distortion and irregularity of the neurofibril network.

In the left optic thalamus the growth was denser, but in general similar to that in the right optic thalamus. The nuclei were slightly larger and more irregular and there was greater variation in the size, shape, and form of the individual cells, many of which showed faint staining of the cell body with van Gieson and eosin stains. In the periphery the cell types were similar to those in the right thalamus, there being present numerous well-defined astrocytic cells and also more mature forms of moderate size. In the centre and hæmorrhagic areas the cells were greatly enlarged, and giant cells with long, coarse, thick processes of every possible shape and form were present (Fig. 13). Some were irregularly astrocytic, others triangular-shaped, and others bipolar. The cell bodies were clearly defined, but not so sharply outlined as those of the more regular-shaped astrocytes in the periphery. Some cells had two nuclei and there was considerable variation in the size of the cells with clearly outlined processes. There were other cells in which no processes were stained. Some of these had clearly defined and darkly stained cell body, but mostly the cell body was indefinite and

irregular. Such cells varied much in size and form. Some had multiple nuclei, and occasionally they occurred in little clumps. There were also many round, oval, or elongated nuclei without any stainable cell body. In some areas the tumour cells were swollen, pale, and faintly stained, with the nucleus frequently compressed and flattened against the side of the cell. Such cells corresponded closely to gemastete







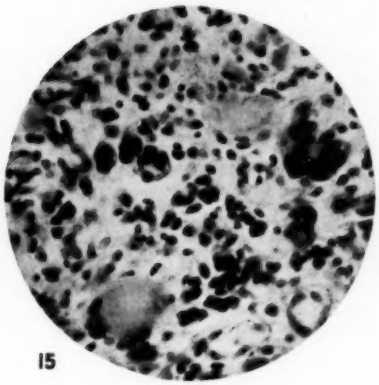


Fig. 12.—Case 3 : From the right thalamus, showing the general gliosis accompanying the growth. (Anderson's Victoria blue.)

Fig. 13.—Case 3 : From the left thalamus, showing the giant nature of some of the cells and the coarse, thick processes which fill the background of the section. (Hortega's S.C.A).

Fig. 14.—Case 3 : From the left thalamus showing the bundles of glial fibres. (Anderson's Victoria blue.)

Fig. 15.—Case 3 : The focus of tumour formation on the right side. (Iron hæmatoxylin and van Gieson.)

cells, being, however, much more irregular in size, shape, and form. There was a variable increase of fine glial fibres throughout the left thalamus. This consisted of a fine network. In some parts it was very slight, but in others it was dense and thick, and parallel bundles of fibres ran along the capillaries (Fig. 14). Foci of calcification were occasionally seen in relation to these vessels.

Although there was gross destruction of essential nervous elements, bundles and isolated myelinated fibres could be traced everywhere, even in the areas of greatest

growth. Only a few nerve cells, however, remained towards the centre of the thalamus, and these were in various stages of degeneration. In myelin preparations the left thalamus was pale, but the internal capsule was darkly stained.

In the area of cellular overgrowth inferior and lateral to the right thalamus, a different appearance was found. Here the cells were closely packed together, forming a distinct tumour mass and completely replacing the normal tissues, leaving only a few scattered nerve fibres and cells round the periphery of the area. The cell nuclei were larger than those found even in the left thalamus, and giant lobulated nuclear masses occurred. Only the giant cells showed faint staining of the cell body with ordinary nuclear stains. With silver stains an irregular and indefinite cell body could be made out round many of the cells. Apart from a few isolated astrocytes no cell processes were stained except slight irregular blunt projections in some of the giant cells. Also there were no neuroglial fibres in the background. The blood vessels showed endothelial proliferation and degeneration of their walls and irregular mitoses were present. Although the cellular mass was sharply marked off from the surrounding tissues, the periphery of the growth was less dense and the marginal cells intermingled with those forming the diffuse overgrowth in the right thalamus. It was, however, distinctive from the diffuse growth found in the thalamus and from its microscopical features must be considered an area of tumour formation having the characteristics of a spongioblastoma multiforme (Fig. 15).

Changes in Other Parts of the Nervous System.—There was present in the upper part of the midbrain a general cellular overgrowth, greater dorsally. This was accompanied by much new glial fibre formation, but it had led to little disturbance in the essential nerve elements. Along the infero-lateral margin of the midbrain on the right side a wide band of increased marginal cellularity was present, comprised mostly of immature spongioblastic cells, but containing many astrocytic forms of varying size and shape. Throughout the remainder of the brain stem there was increased marginal gliosis, and in the dorsal part of the pons and medulla some increase of neuroglial cells showing a greater variation in size, shape, and type than is normally found. Many nerve cells in the brain stem and dentate nuclei showed accumulations of fat in the cell body, especially in the olivary nucleus. The lenticular nucleus was not generally involved in the overgrowth, but in this structure on both sides there was a general increase of neuroglial nuclei, very irregular in shape. The caudate nucleus was less definitely involved. There were very definite pathological changes in the medial aspect of the temporal lobes on both sides. This was greater on the right side, where a moderate cellular overgrowth, greater subpially, extended widely in the hippocampus and uncus. There was also dense marginal gliosis which extended forwards and was very severe round the anterior end of the choroidal fissure, where it involved the optic tract. On the left side, however, there was only slight increase of neuroglial nuclei in the white matter of the hippocampus and medial aspect of the temporal lobe and the marginal gliosis and cellularity round the anterior end of the choroidal fissure was less dense. There were no gross changes in the other parts of the cerebral hemispheres. In different areas foci of marginal gliosis were present and occasional subpial hæmorrhages. There was also irregular thickening of the meninges and small foci of endothelial cell proliferation. Many nerve cells also showed considerable fatty degeneration of the cell body.

Summary and Discussion of the Case

Clinically the case was characterized by a ten months' history of headaches, drowsiness, and such mental symptoms as failure of memory, confusion, and disorientation. Pathologically the predominant feature was the diffuse new growth throughout both optic thalami, consisting of a wide variety of abnormal neuroglial cells in various stages of differentiation superimposed upon the

essential nervous elements and gradually replacing them. All stages were seen, from a slight new formation of small, regular-sized cells in the anterior part of the right thalamus with no alteration in the essential nervous elements, to a dense overgrowth of cells very variable in size, shape, and form replacing practically entirely the nerve cells and fibres in the centre of the left thalamus. Classification of the disease process as a single or even mixed cell glioma does not seem possible. The tumour would have to be considered a mixture of a diffuse astrocytoma, a gemastete cell astrocytoma, an astroblastoma, a polar spongioblastoma, and a spongioblastoma multiforme. The changes in the temporal horns might be considered a spread of the growth into those regions, but the slight pathological changes in the brain stem cannot be so considered, as it is inconceivable that the tumour cells could migrate so irregularly through the tissues from one point of origin.

Like the preceding cases, it must be considered as primarily a diffuse gliomatosis and of similar origin. Here, however, in the centre of the left thalamus there was such extreme rapidity of growth and variability of cell form that the differentiation from tumour formation was difficult. It perhaps could not be made if it were not that a gradual increase in severity of the pathological changes can be traced from other regions of the thalamus. This dense area, however, could be sharply distinguished from the focus of true neoplastic formation, which has developed in the area of growth lateral and inferior to the right thalamus. Here the cells had escaped entirely from the laws that govern normal growth of neuroglial cells, and were clearly growing as a focal tumour. They showed no processes and gave rise to no production of neuroglial fibres, and bore little resemblance to the abnormal neuroglial cells which were present in the diffuse overgrowth. One might regard them as a new race of cells, and the classification spongioblastoma multiforme or glioblastoma can be accurately applied to them. A few of the cells in the very dense areas of gliomatosis were similar to those in the tumour area, and it is difficult to assess their significance. They may indicate a gradual transition to the formation of a spongioblastoma multiforme, or they may be still under the control of normal tissues and capable of further differentiation.

The case, therefore, illustrates in itself different degrees of diffuse blastomatous overgrowth of the neuroglia, and the development in association with this overgrowth of a focus of anaplastic tumour formation. The factors determining the origin and nature of the diffuse growth are entirely obscure, as are also those determining the origin of the autonomous growth.

General Discussion

The three cases which have just been described have been classified as a diffuse gliomatosis of the optic thalamus.

In the first case the cellular proliferation was slow and very fibrillar, and had only led to slight enlargement of the thalamus. In the second case, however, it was more rapid, and a greater variety of abnormal neuroglial cells was present, and very dense new cell formation had occurred in the anterior part of the

thalamus. A moderate gliosis varying in different regions accompanied the growth. In the third case the changes in the right thalamus corresponded closely to those in Case 1, while those in the left thalamus were very similar to those in Case 2, except that cells with large cell body and coarse, thick process were more numerous. An area of gemastete cell development leading to complete obliteration of all nervous structure was present in both. In the third case there had also developed an area of anaplastic tumour formation, so that all stages of blastomatous overgrowth of neuroglial cells were found in these three cases, from a slight overgrowth of practically normal cells right up to the focal formation of a malignant glioma. It seems probable, therefore, that in some cases other types of true tumour formation, e.g. an astrocytoma, an astroblastoma, or a polar spongioblastoma may arise on the basis of a primary diffuse gliomatosis, and may even become the predominant feature of the growth.

The pathological process in these cases is in general similar to that which has been described under the title of " Gliomatosis Cerebri " (Nevin, 1938). In some of the cerebral cases the thalamus was also involved in a diffuse fibrillar or cellular overgrowth, and a feature of the new cell formation in the cerebral cortex was the difference in the fibre production in the grey and the subcortical white matter. This was also present in the island of Reil in the second case of this paper, while other similar features were the perivascular overgrowth and the accumulation of new-formed cells round nerve cells. This pathological correspondence further emphasizes the suggestions which have been put forward with regard to the nature of the thalamic hypertrophy in the present cases, especially the possible developmental abnormality of the neuroglia which may form the basis for the new growth, as the cerebral cases were more closely related to Von Recklinghausen's disease. On the other hand, since each of the cases of gliomatosis of the optic thalamus in the present paper were associated to a greater or less extent with involvement of the brain stem in a manner similar to that found in pontine hypertrophy, emphasis is thereby given to the suggestion already made (Nevin, 1938), that these pontine growths and also gliomas of the optic nerve may possibly arise as a diffuse gliomatosis, and in future might profitably be studied from this angle.

Literature

There are comparatively few discussions of the pathological nature of gliomas of the optic thalamus in the literature. Weil (1933) has described a case of megalencephaly in a boy of six, associated with a diffuse, infiltrating tumour of the optic thalamus, brain stem, and cerebellum. The tumour cells had not led to great destruction of nerve tissue, and although there was some degeneration of myelinated fibres the nerve cells were well preserved. The tumour cells were condensed subpially in the spinal cord and cerebellum, and there were clusters of tumour cells around the Purkinje cells. The author considered the pathology of the cellular overgrowth to be a diffuse glioblastomatosis. The enlargement of the cerebral hemispheres was due to hypertrophy

and not hyperplasia of the neuroglia, and in the areas of tumour growth the neuroglia had become first hyperplastic and later developed into a cellular glioblastomatosis.

Marburg (1906) described a somewhat similar case, except that the hypertrophy also affected the essential nervous elements, and the diffuse glioma was present especially in the thalamus and pons. It can hardly be doubted that in these cases the diffuse new growth has arisen on a developmental basis, and although there is possibly much variation in cell type and differentiation, the main pathological features of the growth are similar to those found in diffuse gliomatosis of the optic thalamus.

Stern (1937) has described a case in which a glioma of the optic nerve was associated with a diffuse tumour of the optic thalamus on the same side. The tumour cells in the thalamus were in the main bipolar spongioblasts, and she classified the case on an embryological basis as a spongioblastoma polare. She has kindly allowed me access to her preparations, and while the growth should be labelled a spongioblastoma polare if an embryological classification is attempted, its diffuse nature with the preservation of the essential nervous elements admit of the possibility that biologically it had arisen as a diffuse gliomatosis.

It is not suggested that all gliomas of the optic thalamus are in their essential nature a diffuse gliomatosis. Localized tumours of one or other type may arise. Some of these which have been studied, however, have shown a marked heterogeneity of cell structure. Baasch (1937) studied a glioma of the thalamus, aqueduct, and pineal region in a youth of seventeen. The cell picture in different places exhibited different stages of cell differentiation, and he considered the tumour to have arisen partly diffusely and partly in a circumscribed manner in an extensive subependymal embryonal layer. This possible pathogenesis is closely related to diffuse gliomatosis but in the latter condition the cells of origin, whether mature or undeveloped, must be considered to have migrated much farther from the position of the embryonic neural tube than the subependymal region. Baasch's case therefore supports the possibility that some more or less localized gliomas of the optic thalamus may arise on the primary basis of a diffuse gliomatosis. In any case, it is clear that all these diffuse growths in the thalamus must be studied not from the point of view of their classification according to the predominant type of cell found, but as a biological abnormality of the neuroglial system, and clues to their histogenesis may be found in the surrounding or even distant neuroglia.

Scherer (1937), in his study of gliomas of the cerebral hemispheres along these lines, has found an extraordinary variation in cell form in these growths, and he has considered that in some tumours there can be distinguished two sets of structures, the essential structure of the tumour and the secondary structures developed by the interaction of the neoplastic process and the invaded tissue. These secondary structures are such features as the clumping of tumour cells around nerve cells, along the vessels underneath the pia, and the gradual infiltration of the cortex. He can trace in some tumours from the periphery to the centre a gradual increase in new cell formation with increasing cell de-differ-

entiation till in the centre of the tumour its essential structure is found having little resemblance to neuroglial cells. These secondary structures in Scherer's sense are features which characterize diffuse gliomatosis whether in the thalamus or in the cortex, so that the study of the essential nature of diffuse new growths in the nervous system is of importance from the point of view of gliomas in general. It seems unlikely that a tumour cell once having escaped entirely from the laws that govern normal growth could even by its interaction with normal tissue produce cells more akin to normal neuroglial cells. This may take place, but the possibility exists that growths showing marked secondary features in Scherer's sense may arise as a diffuse gliomatosis with anaplastic tumour formation predominating at the time of death. The other possibility exists that once a malignant glioma has developed, chemical substances liberated therein may diffuse into the surrounding tissue and cause a blastomatous reaction locally in the adjacent neuroglia, which would then be considered not as an interaction of spreading tumour cells and normal tissues, but as a blastomatous reaction of the normal neuroglia to a malignant growth. These observations only emphasize the point already made in reference to the optic thalamus that all gliomas must be studied as biological abnormalities of the neuroglia, and not simply with a view to classifying them as tumours arising from one or other type of embryonic cell.

Summary

Three cases of diffuse gliomatosis of the optic thalamus have been described. The histogenesis of this type of new growth and its possible relationship to the development of gliomas in general have been discussed.

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I wish to thank the physicians who have allowed me to publish their cases. My thanks are also due to Professor Pulvertaft for permission to take the microphotographs.

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CRITICAL REVIEW

THE TECHNIQUE AND APPLICATION OF ELECTRO-ENCEPHALOGRAPHY

BY

W. GREY WALTER

THE rate at which scientific knowledge is accumulated depends upon a number of factors the relative importance of which is not the same in the various branches of science. The history of physiology and medicine suggests that their development is becoming increasingly dependent upon the progress of the physical sciences. This is not merely because the physiologist and clinician prefer to describe their observations in physical and chemical terms ; the link is apparent in the first stage of the scientific method, the manner in which the observations are made. The number of new facts discovered with the unaided senses grows smaller ; the range of perception is extended by more and more elaborate tools. This growing dependence of the biologist on the physicist is familiar, but it has been emphasized here because it suggests some reasons for the difficulty of integrating the facts collected in the last ten years by many observers of the electrical activity of the human brain.*

The use of modern electrical techniques in electro-physiology has made the collection of facts easier and more rapid, but the subjects in which the facts have been most satisfactorily built into a coherent theoretical structure are those which were most developed before the introduction of the new methods. In lines of study which spring directly from technical advances the tendency is for more problems to be created than can be solved ; worse still, the avalanche of new observations produces a chaos in which a problem can be stated only in the most indefinite terms. An atmosphere is soon created which is congenial to empiricism and deductive speculation ; while the ascetic principles of inductive logic are forgotten in the search for facts and applications. The apparent incoherence of the factual premises is likely also to lead to a cynical individualism in the attitude of the various workers toward their subject, and variations of method and terminology arise which make it hard for those who should be colleagues to understand one another, and almost impossible for a new-comer to understand any of them.

The short history of electro-encephalography illustrates this process in detail. The electrical phenomena associated with nervous activity were observed almost as soon as there were instruments capable of detecting them, early in the last century, and Caton (1875) showed that electrical changes

* The reviews by Jasper (1937) and Fessard (1938) were found most useful as guides to the literature.

occurred in the exposed brain of an animal both when resting and during stimulation and motor activity. Fleischl von Marxow (1883), Beck (1890), Gotch and Horsley (1891), and several others contributed information which suggested that the central nervous system of animals possessed electrical properties related to those found in peripheral nerve and muscle. Prawdicz-Neminski (1913, 1925) described six types of wave in what he called the " electrocerebrogram " of the dog, and was the first to attempt to classify his observations.

The experiments of all these workers were made on the exposed brains of animals, using galvanometers to detect slow changes and string galvanometers or capillary electrometers for the rapid ones. The comparative lack of interest in the electrical activity of the brain may seem surprising until it is remembered that the electrophysiology of nerve and muscle was still in its infancy, though rapidly developing, and the clearer problems of excitation and propagation in these simpler tissues afforded ample scope for those whose interest was attracted to such subjects.

In 1929 Berger published the first record of the electrical activity of the human brain. This was taken through the unopened skull with a Siemens galvanometer, and the deflections were therefore small and unconvincing. For this reason, and perhaps also because he was known to have been looking for the phenomena he described, Berger's " elektrenkephalograms " were almost disregarded and his entirely original, painstaking work received little recognition until Adrian and Matthews (1934) supplied thorough respectable confirmation. By this time Berger had published eight papers ; since 1932 his records have been with an amplifier and oscillograph, and he has applied his technique to the study of many pathological conditions. He also worked out a theory to account for his observations, and this will be discussed later.

Since Adrian and Matthews confirmed that, given adequate technical equipment, the electrical waves of the human brain could be observed with less trouble than the action potentials from the single nerve-fibre preparations of modern electrophysiology, electro-encephalography has become one of the most popular laboratory subjects. The normal electro-encephalogram was soon found to be, in Adrian's phrase, " disappointingly constant," and the attention of many workers was diverted to the study of nervous disease. This was found a rich field, and the surprising state has been reached wherein what may be called the electropathology of the brain is further advanced than its electrophysiology ; while there is still a great variation of opinion as to the precise nature and significance of the features of the normal electro-encephalogram, its usefulness in the study of diseases of the brain is widely accepted.

A body of knowledge which comes into existence in this way, rather from the technical ease with which it was begotten than from its necessity in the general scheme, is likely to suffer not only from congenital deformities but also from the further handicap that if a large number of observations are made in a short time, some of them are likely to be false ; and when the observers are armed with a weapon as powerful as the equipment used in electro-encephalography, the errors may be greatly magnified ; so that it becomes hard enough to sift true from false, let alone compound the true into a consistent and enlight-

ening whole. Just as in microscopical anatomy the fixation of a tissue or the aberration of a microscope may produce artefacts which mislead even experienced histologists, so in electro-encephalography both the subject and the apparatus may produce spurious electrical discharges which are almost indistinguishable from those associated with the brain. Accordingly, the requirements and limitations of the technique will be discussed before considering the information which it has yielded.

Technical Considerations

The upper limit of size of the brain potentials as led off through the skull approaches that of the electrocardiogram ; about one millivolt and potentials even greater than this are obtained when leads are placed directly on the exposed cortex. Discharges of this magnitude are rare, however, and in fact are only found in abnormal conditions. The commonest features of the human electro-encephalogram (E.E.G.) usually have a potential of less than 50 microvolts, and significant discharges can be recognized which are as small as 5 microvolts. If there were no limit to the amplification which could be used, even smaller cerebral potentials might be detected, but for physical reasons the greatest sensitivity which can be used is such that an input of 5 microvolts produces a measurable deflection of the recording instrument, which should be capable of responding at the same time to an input of twenty times this size without damage or adjustment. The time relations of these small potentials are, by ordinary physiological or electrical standards, very slow ; their effective duration varies from one second down to perhaps 20 milliseconds. Sometimes they are rhythmic, sometimes they occur as pulses or transients. Rohracher (1935, 1937*a*) has described frequencies as high as 1,000 per second associated with intellectual activity, but their existence has not been confirmed. Even more doubtful are the discharges reported by Cazzamalli (1936, 1937). These are claimed to appear during emotional excitement and have a frequency of the order of megacycles !

There is no oscillograph or galvanometer capable of dealing unaided with such potentials, and thermionic amplification is essential ; even then careful design is necessary, for the frequency-band on which the brain appears to work, having no æsthetic or commercial importance, falls below the range of the conventional audio-frequency amplifier. The ideal arrangement would be a direct-coupled amplifier with a circuit such as that described by Matthews (1938). This will reproduce faithfully all frequencies, even steady differences of potential, and has the added advantage that it cannot be choked by overloading with a very large transient at high sensitivity. The very virtues of this system, however, make it tiresome for electro-encephalography, since with electrodes on the skin, slow swings of potential are picked up. These are often of considerable size and when amplified would result in violent base-line fluctuations. For most purposes a condenser-coupled circuit can be used provided that the overall time constant is not less than one second.

For reasons which will be discussed later, it is generally necessary to use several independent channels of amplification at the same time, therefore particular attention must be paid to the input stage. Amplifiers in which one side of the input is a common earth line cannot be truly independent, so a " balanced " input stage must be used. There are several possible arrangements, but the simplest is probably that described by Matthews (1938) and originally due to Tönnies. Like the earlier circuit designed by Matthews (1934), this is relatively immune to radiated interference, such as that from alternating current mains, so that in most cases elaborate screening arrangements can be dispensed with. It has the considerable practical advantage that the batteries, being earthed, can be common to the several channels, and that the subject too can be at earth potential and may therefore be touched without producing electrical disturbances. In electro-encephalography the parasitic potentials set up in the subject's skin and in the electrodes are usually greater than the valve noise of the amplifier,

and the base-line may legitimately be smoothed considerably by filtering out the audio-frequency components of the background noise which lie above the highest frequencies produced by the brain. None the less, it is sound practice to have as quiet a first stage as possible. The special " quiet " triodes, Marconi A537 and MH40, are specially suitable. The input leads and early stages of the amplifiers should, of course, be electrostatically screened.

The output from a balanced input stage has one side earthed, and thereafter a conventional design may be adopted. The amount of amplification necessary depends, of course, upon the sensitivity of the recording system. This may be of any type provided that it will respond faithfully at the frequencies concerned and permit continuous observation or visible recording over a long period. Whatever type of oscillograph is used, it is important that provision be made for multiple-channel recording. Mirror oscillographs have been used by many workers. (For example, Berger, 1930 *et seq.* ; Adrian and Matthews, 1934 ; Jasper and Andrews, 1936.) These are relatively cheap and are convenient for multiple recording. Their disadvantages are that they require a power output stage and that observation of the slow waves by the usual rotating mirror system is unsatisfactory, since at these speeds visual persistence fails to give the illusion of a standing wave. The cathode-ray oscillograph is a highly satisfactory instrument for use with photographic recording. Multi-channel records may be obtained either by using several tubes with mirrors (Walter, 1937) or by commutation of the several channels on to one tube (MacMahon and Walter, 1938). Old-fashioned gas-focused tubes may be used, and these require only about 50 volts output and negligible power from the amplifier. Recently double trace (Cossor) and triple trace (Western Electric) vacuum tubes have been produced, and these would be ideal for electro-encephalography. Tubes fitted with an afterglow screen make the form of even the slowest deflections easily visible. Provided that frequencies above about 30 per second are not encountered, the ink-writing oscillograph is by far the most convenient, particularly when long records are taken. The " Polyneurograph " of Tönnies (1933), which has five writers, each with a natural frequency of about 50 per second, is probably the finest equipment of this type, but it has not been manufactured commercially. The piezo-electric writer of Offner and Gerard (1936) has a higher natural frequency than most electro-magnetic systems, but the size of the deflection obtainable with it seems rather small. The " undulator " of Garceau and Davis (1935) has given excellent results and a four-channel instrument of similar type has been used by Gibbs, Gibbs, and Lennox (1938) for some years in their studies of epilepsy. The peculiar advantage of writing oscillographs for continuous recording is illustrated by the work of Loomis, Harvey, and Hobart (1935) on sleep, in which continuous records were taken for periods up to eight hours. Most ink-writing oscillographs are very expensive and naturally require considerable power, but a simple and cheap way of obtaining a direct record is to adapt a moving-coil loud-speaker or relay for tracing on the smoked paper of a kymograph. This device was used by Golla, Graham, and Walter (1937) for the study of a number of epileptic patients. With a large kymograph, recording can be carried on for about thirty minutes.

The details of the recording apparatus, then, are unimportant, providing that the following four conditions are fulfilled :

1. Sensitivity must be such that an input of 5 microvolts will produce a measurable deflection.

2. The response must be uniform and undistorted from a frequency of one cycle per second up to 50 cycles per second, and should not be grossly deficient for some way beyond these limits.

3. Several recording systems should be used simultaneously, and must be entirely independent of one another.

4. Facilities must be provided for continuous observation and recording.

Another technical matter in which there has been considerable variation, but which is not actually very important, is the type of electrodes used and the manner in which

they are held on the head. Berger's original records were taken with silver wires inserted into the scalp under local anæsthesia with the help of ground-down hypodermic needles. This proceeding has not been found to have any particular advantage, and of course is positively dangerous when the subject is uncoöperative. Berger himself now uses silver foil and cotton-wool moistened with saline, held on with rubber bands. An elaborate and theoretically sound electrode was described by Jasper and Andrews (1936), but they have abandoned this (1938) for a simpler design consisting merely of chlorided silver and felt and stuck on the scalp with collodion. A similar pattern was described by Walter (1936) and the silver-silver chloride pad seems the most practical form for ordinary purposes. These are not truly non-polarizable, but if they are regularly chlorided and kept out of direct sunlight, they produce no visible distortion of the brain potentials and generate only a minute e.m.f., which is important if no blocking condensers are used in the leads to the amplifiers. The attachment to the scalp depends upon the type of observation which is being made. For a long session the electrodes must be moistened with jelly saline and stuck on firmly with collodion, but for shorter studies they may be held in place with a hairdresser's wave-setting cap and dampened with saline as described by Walter (1937). This method is quick and flexible, but is unsuitable if the subject is likely to move a great deal or if rapid drying of the pads is likely. In any case, the grease of the scalp should be removed with alcohol from the places where the electrodes are to be applied. The hair need not be shaved, but care should be taken that the electrode is in firm contact with the skin. If the scalp has been recently shaved or if electrodes have been placed in a great many positions, the natural insulation of the sebum will have been entirely removed and replaced with a film of electrolyte which, by considerably lowering the inter-electrode resistance, can produce an apparent reduction in size of the potentials. If observation has to be continued in these circumstances, the scalp must be liberally rinsed with water and a small quantity of vaseline rubbed in between the electrodes. In general it may be taken that whatever pattern of electrode is used it should be relatively non-polarizable and should not hurt the subject.

For leading off directly from the human cortex, wick electrodes may be used, or, for localizing, a small concentric silver electrode is convenient and if held in an anglepoise holder can do no damage to the tissue.

The manner of leading off has a great effect upon the results obtained and the interpretation which can be put upon them. When Berger's discoveries first came to be taken seriously, a dispute soon arose as to the respective merits of " Bipolar " and " Unipolar " leads. Berger's arrangement was bipolar, consisting of one electrode on the forehead and one on the occiput, thus including most of the brain between the electrodes. Adrian and Matthews (1934) also used bipolar leads, but with an important difference which will be explained later.

Tönnies (1934) pointed out that with both electrodes equally near to presumably active cortex, a complex record would be obtained due to all the discharges originating in the large mass of tissue, and advocated an " indifferent " electrode attached to the two ears with an exploring electrode on the scalp. With multi-channel recording the indifferent-ear electrode is connected to the common earth line and the exploring electrodes are placed over the parts of the brain which are to be studied. Location of the discharges is accomplished by comparing the size of the deflections from the various channels, presuming that the amplification is exactly the same in all and that the potentials picked up by the electrode nearest the active area are always larger than those picked up by electrodes further away from it. This argument seems fairly convincing and unipolar leads have been used successfully by many observers, including Gibbs, Davis, and Lennox (1935), Gibbs, Lennox, and Gibbs (1936), Gibbs, Gibbs, and Lennox (1937), and Loomis, Harvey, and Hobart (1935 *et seq*).

There are certain fallacies, however, in the argument for unipolar leads, the two chief being, first, that no electrode position is truly indifferent, since no part of the head is either infinitely far from the brain or in contact with the inside of it (as is the

" indifferent " electrode used for obtaining monophasic action potentials from nerve or muscle), and secondly, that, treating the brain and its envelopes as a source of potential and an ohmic resistance network respectively (*cf.* Tönnies, 1933), the potential developed between two points (the electrodes) is a function not only of the resistance (or distance) between one of the points and the potential source, but also of the resistance between the points. In practical terms this means that in the first place some electrode arrangements will result in the " indifferent " electrode being nearer to the point of activity than any of the " active " ones, and in the second place the active electrode which seems to be picking up the largest potentials may be doing so not because it is nearest to the focus of activity but because it is furthest from the common indifferent electrode. The situation is made even more difficult by the fact that the electrical discharges of the brain are not always in the same sense as are those of nerve and muscle, in which an active or injured region is always electro-negative to an inactive or normal one. This irregularity makes location virtually impossible with only one channel. A technique to overcome these obstacles was devised by Adrian and Matthews (1934) and perfected by Adrian and Yamagiwa (1935). With it they were able to prove that the focus of origin of Berger's " alpha rhythm " was usually in the occipital region and that it wandered over an area of several centimetres. By placing a source of feeble alternating potentials inside the skull of a cadaver they were able to show that location was possible to within a centimetre. The method involves the use of three or more separate channels, each starting with a " push-pull " or balanced input stage. If three channels are used the input leads are connected to four electrodes in such a sense that a potential change at an electrode common to two of the channels will produce deflections which are out of phase in the two channels. Location of a focus of activity is achieved by observation of the phase relations of the deflections in the several channels, and the accuracy is equal roughly to the distance between the electrodes. This technique has been used for the location of cerebral tumours by Walter (1936, 1937, which contains illustrative diagrams), for the location of abnormal foci in epileptics (Golla, Graham, and Walter, 1937), and to determine the region of onset of cardiazol convulsions (Cook and Walter, 1938).* It appears to be the most trustworthy method of location available at present, though it has certain disadvantages. The chief of these, which is absolute rather than relative to other methods, is that, as stated above, the record from any one channel represents the electrical activity of the tissue in the neighbourhood of both electrodes. If sufficient channels are used, the discharges may be sorted out by analysis of the records, but this becomes very laborious when there are more than two active foci or when there is a generalized discharge.

The last matter to be considered before discussing the electro-encephalogram itself is the recognition of various distortions and artefacts. Distortion of the brain potentials by the amplifiers and oscillographs can be avoided only by observing the physical rules of thermionic amplification and by allowing for the properties of the recording system used. For example, the valves must be worked on the linear portion of their characteristic curves, and the oscillograph, if mechanical, must be critically damped and have a natural frequency above that of the fastest component of the discharges to be studied. These conditions are, of course, the same whatever the subject of investigation and need not be specially considered here.

The chief sources of artefacts in electro-encephalography are seven in number.

1. Radiated interference. The various forms of this can only be learned by experience and are most easily tracked down with a portable radio set. The balanced input reduces them considerably, but in some cases the subject has to be enclosed in a screen. The radiation from diathermy apparatus is probably the worst form. Movement of any electrostatically charged body, such as a rubber tube or celluloid ruler,

* The "triangulation" sometimes used by Jasper and Hawke (1938) (in which three channels lead off from three electrodes placed so as to form a triangle around the area under observation) is essentially the same method, and owes little to trigonometry.

in the neighbourhood of the input will produce large deflections unless the subject is earthed, as is possible with the input circuit recommended above.

2. Movements. The extent to which these interfere with recording depends upon the method of electrode attachment, since their transformation into electrical potential changes depends upon variation of electrode contact resistance. To lessen the drag upon the electrodes the leads to the amplifiers should be light and may conveniently be suspended from a flexible stand. If violent movements of the jaw or scalp or convulsions are expected, the electrodes should be held on the scalp with collodion or surgical strapping, but for ordinary purposes a cap is adequate.

3. Photo-electric potentials. Most metallic electrodes either change their resistance or develop an e.m.f. when exposed to light, and silver-silver chloride exhibits this property. For this reason the damp part of the electrodes should not be exposed to light of fluctuating intensity, particularly if the effect of this upon the brain potentials is to be studied.

4. Skin potentials. A small, steady e.m.f. exists between any two electrodes placed on the skin, due to slight differences in polarization and differences of ionic concentration in the tissue fluids and the electrolyte used. These steady potentials will only interfere if the resistance of the electrode system changes owing to movement or drying of the electrodes, both of which should be avoided. In some subjects the so-called " psycho-galvanic reflex " can be picked up from the scalp, and since conditions which produce this reflex also tend to affect the brain potentials, this source of error should be controlled by taking simultaneous records from the hands when any doubt arises.

5. Blinking of the eyelids is probably the commonest single source of artefacts. The potentials are very large—several hundred microvolts, and in nervous subjects may be rhythmically produced. They can, however, be easily recognized, since they are always in the same sense for a given direction of movement. Flutter of the eyelids produces a large quasi-sinusoidal discharge which can be recognized as an artefact only by localizing in the same way as any other potential is localized, or by recording the lid movements by some other means. Movements of the eyeballs are also frequent sources of confusion, and are probably an associate cause of the blink artefacts. This phenomenon may be put to use for recording nystagmus. It is particularly prominent in certain classes of psychotic patient as an habitual movement, and in these cases the movements sometimes are very difficult to detect by inspection of the eyeball. Potentials which seem to originate from the extreme frontal pole should be suspect until they are proved not to be eye-artefacts. One helpful point is that the eye movements are nearly always conjugate, though the lids may, of course, be winked separately.

6. An artefact of uncertain origin is a small rhythmic discharge which can sometimes be detected in the fronto-temporal region. This is in rhythm with the heartbeat and occurs at the same moment as the pulsation of the arteries of the head. It is usually best seen in cases of hypertension, but is not apparently due directly to the mechanical effects of the pulse, since electrodes placed on the radial artery where the pulsation is much greater are not similarly affected. It is not an electrocardiogram, since by simultaneous recording this can be shown to be over before the artefact occurs. From its position on the head it seems probable that it is associated in some way with pulsation of the middle meningeal artery, but further study is required. When better understood it may conceivably be found useful as a criterion of the effective intracranial arterial pressures.

7. The last class of artefact is that due to bio-electric potentials. Nerve action potentials are too small and far away to influence electrodes for electro-encephalography, but muscle action potentials are nearly always present to some extent, particularly in records from the frontal region. Their presence helps to identify potentials due to movement of the scalp and clenching of the jaws, which are not easily noticed. The time relations of these potentials are usually much shorter than those of the brain potentials, and they can therefore be eliminated by electrical filter circuits. In very powerful tonic contraction the almost synchronous volleys of action potentials may

produce a smooth, rhythmic discharge which would be hard to distinguish from some of the brain rhythms were it not always accompanied by a considerable amount of asynchronous activity in the form of a small, rapid discharge of sharp spikes. The electrocardiogram is practically never seen with electrodes on the head, since the neck tends to form an iso-electric isthmus.

The spurious potentials from these various sources have naturally been remarked on by most observers, but they are responsible for a certain number of fallacious statements, and constant vigilance is necessary to exclude them from electro-encephalographic records, the features of which may now be described.

The Electro-Encephalogram

Berger's first papers described two electrical rhythms. The first, which he called " alpha waves " and which was referred to five years later by Adrian and his collaborators as the " Berger rhythm," consists of an almost sinusoidal discharge with a frequency of about 10 per second and with a potential varying irregularly from zero to about 100 microvolts in some subjects. With his five years' start, Berger was able to build up without dispute a theory to account for his observations on both normal and abnormal subjects, and for the reasons mentioned earlier his attitude was conditioned to a great extent by his preconceived notions and the shortcomings of his technique. Nevertheless, the priority in nearly all the problems connected with electro-encephalography is certainly his, though his opinions are not shared with the majority of those who have followed him. Strange though it may seem, the extreme, perhaps excessive, simplicity of his methods led to a puzzling indefiniteness and complexity of theory. The explanation for this is that since he used only one channel, and placed his electrodes as far apart as possible on the head, his records are of what has been called the " global " electro-encephalogram, that is, they show the electrical activity of the brain as a whole. Berger's conviction that the rhythms which he found represented a basic function of the whole cortex was strengthened when he found that approximation of his electrodes reduced the size of the potentials. Such a reduction in size could, of course, have been foretold from Ohm's law, and has no other theoretical significance. Since, moreover, the rhythm of each individual was characteristic both in rate and regularity and seemed to him adversely affected more by general psychological factors such as nervousness and attention rather than by any specific sensori-motor activity, Berger considered it reasonable to build up a hypothesis of the significance of the alpha rhythm in terms of a holistic theory of central nervous action. The difficulty of understanding the theoretical portions of his later papers is partly responsible for the general scepticism regarding the facts which Berger was attempting to explain, and the impression made by his work was confused by his neglect to attempt the second process of the inductive method, that of classification of his observations. When Adrian and Matthews (1934) and Adrian and Yamagiwa (1935) had verified the existence of the alpha rhythm they compared it to the spontaneous electrical rhythms which Adrian had previously demonstrated in the central nervous systems of various animals (Adrian, 1930*b*, 1931, 1932 ; Adrian and Buytendijk, 1931) and in injured mammalian nerve fibres (Adrian, 1930*a*). By classification with these phenomena the alpha rhythm gained in respectability what it lost in strangeness,

though only a most tentative explanation could be given of the rhythmic activity even in the nervous system of a caterpillar.

In the subjects who happened to be used by Adrian and his colleagues one property of the alpha rhythm, which has since become a classical demonstration, was particularly well marked. This is its inhibition by visual activity. Furthermore, unlike Berger, Adrian was able to locate the focus of the alpha discharge, which in his subjects was restricted to the parieto-occipital region of both hemispheres. He also confirmed Berger's discovery that the rhythm was decreased or abolished, even when the eyes were shut, by intellectual concentration such as that required for mental arithmetic, and also by a startling noise or sensation. These facts suggested that the alpha rhythm was a sign of physiological rest in the occipital cortex in the neighbourhood of Vogt's Area 19, which is supposed to be associated with the integration of sensation and particularly of visual stimuli. The mechanism of the discharge was supposed to be fundamentally the same as that proposed for the slow bio-electric rhythms in other organs ; the electrical summation of slightly asynchronous volleys of action potentials, the rhythm of these volleys being set by some pacemaker either in the cortex or elsewhere. This hypothesis is still by no means out of court, although many new facts have been collected since it was first put forward, and it has the great merit that no special assumptions need be made about the properties of central grey matter.

The focal nature of the discharge may be accepted since it has been confirmed by all workers who have used suitable equipment. Discharges resembling the alpha rhythm are not restricted to the occipital regions, however, even in normal subjects. Jasper and Andrews (1938) report that in a few subjects a frontal alpha rhythm is more prominent than an occipital one and is not " blocked " by visual activity. There are certainly great variations in the size of the focus, both between individuals and in the same individual from time to time, but a precentral focus is extremely rare among normal subjects. In the author's experience, which includes the observation of upwards of 1000 subjects, normal and otherwise, only four cases have been found to have an alpha focus in the precentral regions and these were all either in pathological conditions or normal subjects in unusual circumstances. The foci in the two hemispheres are nearly always symmetrical and the rate is usually the same on both sides, and moreover the waves are in phase in both foci. Fluctuations in size, either spontaneous or induced by stimulation, are also the same on both sides, which seem to be closely linked. It must be supposed, therefore, either that one hemisphere drives the other, or that both are regulated by a common pacemaker or escapement. Of these two possibilities, the latter seems to fit in better with the fact that the discharges on the two sides are exactly in phase, for a slight delay would be expected if one side were driven by the other. Very little is known, however, about resonance in the central nervous system, and if two areas were accurately tuned to the same natural frequency only a small amount of " feed-back " would be necessary to keep them in phase, and if the synchronization were accomplished by nerve impulses in the callosal white matter, the delay would be very short.

The " blocking " of the alpha rhythms by visual stimuli offers an excellent subject for study. Durup and Fessard (1936) report that an interval of from 0·1 to more than 0·5 second elapses between a visual stimulus and the disappearance of the waves. The latency varies with the intensity and duration of the light stimulus and the relationship is logarithmic over the middle range. This has been confirmed by many observers, notably Jasper (1936), Jasper and Cruickshank (1936, 1937), Loomis, Harvey, and Hobart (1936). These workers report also that the latency of inhibition of the alpha rhythm is shorter than the motor reaction time measured simultaneously. The reaction times in these experiments seem very long, however (0·45 second average in Jasper's work and 0·35 second in that of Loomis, Harvey, and Hobart), compared with the usual figure of 0·1 to 0·2 second, and in the experience of the author the reaction time has nearly always been found *shorter* than the blocking time of the alpha rhythms —a great disappointment, since it had been hoped to discover a sign of activity midway between the afferent and efferent paths. If a movement can be made in response to a visual stimulus before the alpha focus is aroused, the region of this focus must be in the nature of a detour for the impulses concerned. In these unpublished experiments the latency was found to vary by more than 100 per cent. in the same individual in the same conditions.

As mentioned before, the frequency of the alpha-rhythm is remarkably constant in each individual, and provided normal health is maintained does not vary by more than 5 per cent. to 10 per cent. over a period of years (Berger, 1930 ; Davis and Davis, 1936 ; Loomis, Harvey, and Hobart, 1936 ; Jasper and Andrews, 1936 ; Travis and Gottlober, 1937). Berger (1932) found no activity in infants under one month old, and an alpha rhythm with adult features is not seen until the age of 5 or 6 years ; until that time the discharge is slower, and is first seen at about one year as an irregular sequence of waves at about 6 per second which resembles more the E.E.G. of sleep and some pathological states in adults. In an unpublished series of observations on the E.E.G. of people of all ages, Golla, Graham, and Walter found that if the alpha frequencies are plotted against the ages, a smooth, flat-topped curve is obtained ; the plateau extends from about 10 years to 65 years and the drop at both ends is fairly abrupt. Ontogenetically, then, the alpha rhythm starts typically as a discharge at about 6 per second in the early years of childhood, and rises steadily to a maximum frequency of 8 to 13 per second, at which it remains constant until in old age it again declines to about 6 per second, even if the individual retains his faculties more or less unimpaired.

Individual differences between mature subjects are, it should be repeated, very great, and observation of a few people, particularly if they happen to belong to any well-defined psychological or even racial group, may supply misleading data. The various controversies and disputes about the nature and significance of the alpha rhythm may be traced to this fact, and a good example is found in the opinions expressed by different authors on the E.E.G. in blind persons. Impressed by the dramatic inhibition of the alpha rhythm by visual stimuli in their few subjects, Adrian and Matthews (1934) postulated a specific connection between pattern-vision and this inhibition. They were therefore

not surprised when they found the alpha rhythm to be absent in the blind subjects whom they tested, and explained this by supposing that the visual cortex in a person who had been blind since birth or for some years could never have the same function as that of a normal person who was only temporarily in darkness. Berger (1935), however, published quite normal alpha rhythms taken from several blind subjects, and pointed out that in the peculiar circumstances of an electro-encephalographic examination a blind person, being unable to see what was being done to him, would be in a state of greater anxiety and apprehension than a normal subject, and that therefore greater care must be taken to allay his fears and gain his confidence, so that he could reach the state of general emotional and intellectual relaxation necessary for the appearance of an alpha rhythm, and which Adrian and Matthews' normal subjects, being mostly accustomed to laboratory methods, had easily attained.

The existence of an alpha rhythm in the blind can easily be verified, and it has been shown by Loomis, Harvey, and Hobart (1936) to be very easily " blocked " by an auditory or tactile stimulus. In an experiment of the author on a congenitally blind youth the alpha rhythm was found to be easily and regularly suppressed by the silent opening of a door which produced no change in the sound-level detectable by those unaccustomed to use such clues in their daily life.

In general, the conditions in which the alpha rhythm is found are those which for the subject in question imply the least degree of stimulation, interest, and anxiety. The onset of sleep, however, is associated with a fall in frequency and finally with disappearance of the alpha rhythm. The discharge may be inhibited by almost any internal or external stimulus to an extent varying enormously in different subjects. A homely example of the efficacy of internal stimuli is the " cat-box " effect described by Rheinberger and Jasper (1937) in their study of the discharges in the cat's brain. The desire to defœcate or urinate was reflected in a suppression of the spontaneous rhythms. A similar effect can be seen when young children are being examined in such circumstances. The most effective unconditioned stimuli are usually those with the greatest significance or " arousal value " (Jasper, Cruickshank, and Howard, 1935 ; Bagchi, 1937), but the inhibition is easily conditioned, and such conditioning obeys the classical laws of conditioned reflexes ; such phenomena as extinction and time reflexes may be demonstrated, and this is a subject which would probably repay the patient experimenter. Thus, by treating the inhibition of the alpha rhythm as a " response," it may be used to some extent to study a subject's " type " and idiosyncrasies. In this it resembles in some ways the " psycho-galvanic " skin reflex (*cf.* Forbes and Andrews, 1937).

Conditions in which the alpha rhythm is extremely prominent usually border on the pathological, and in the author's experience, those cases which have presented an alpha discharge which was both large in size and resistant to inhibition have complained either at the time or later of some nervous or mental symptoms. This subject will be approached later from the direction of the pathology of the E.E.G.

The possibility of controlling the frequency of the alpha rhythm by inter-

mittent visual stimulation was suggested by Adrian and Matthews (1934). They showed that when some subjects looked at a large, brightly lighted, flickering field, rhythmic potentials could be recorded from the occipital region which followed the flicker frequency up to about 25 per second. This has been confirmed by several experimenters (Durup and Fessard, 1935 ; Loomis, Harvey, and Hobart, 1936 ; Jasper, 1936). Whether this phenomenon should be described as " driving the alpha rhythm " (Adrian and Matthews) or as a succession of the " on " and " off " effects observed by Jasper and Cruickshank (1937), and whether these two descriptions are not the same cannot yet be decided. Jasper (1937*a*) and Jasper and Andrews (1938) stated that potentials can be detected from the occipital region which follow flicker frequencies up to 60 per second and they explained this (1937*b*) with the help of the concept of " alternation." Taking the mean amplitude of the spontaneous alpha rhythm as unity, the size of the evoked potentials was one half at twice the alpha frequency, one quarter at four times, and so on, while at frequencies midway between multiples of the fundamental frequency the response was greatly diminished, suggesting some sort of harmonic response. The significance of these findings cannot be assessed until they are confirmed, since the possibility of confusion with artefacts is considerable owing to the small size and high frequency of the evoked potentials.

Hoagland (1936, *a*, *b*, *c*, and *d*) has shown that the alpha frequency rises with an increase of bodily temperature, and Jasper (1936) and Jasper and Andrews (1938) have confirmed this. The critical thermal increments appear to be from 7000 to 8000 calories, but the accuracy possible in the measurements is not great enough to give the calculation much significance.

Although the alpha discharge is by far the most prominent feature of the normal E.E.G., it is not the only one. Berger has described and discussed rhythms of a frequency of 20 to 25 per second and has called them " beta rhythms." In certain of his records by his own admission these have been radiation artefacts and Walter (1937) has pointed out that artefacts due to electromyograms often give rise to similar rhythmic potentials. This is particularly evident when a recording instrument is used which has a low natural frequency, such as a writing oscillograph, for its response to a series of transients each with an effective frequency higher than its own will be a small oscillation at its own frequency. The same criticism applies to records taken with tuned amplifiers, for the more efficient a resonant circuit, the more it will tend to produce oscillations at its own frequency in response to transients. Wrinkling the brow and clenching the jaws can produce a very good imitation of a beta discharge, even with high-frequency oscillographs, and in the author's experience the beta rhythms found in most records taken without special precautions are spurious. When, however, they appear in records taken by experimenters with a full knowledge of the sources of error and ways of controlling them, their true existence as a character of the E.E.G. cannot be doubted. Marinesco, Sager, and Kreindler (1938*c*) suggest that the beta rhythm is due chiefly to layer V of the precentral cortex, since it is absent in cases of amyotrophic lateral sclerosis, when this layer is degenerate. Jasper and Andrews (1938)

have made a special study of the beta rhythms. They conclude that they are the predominant components of the precentral E.E.G., have an average frequency of 25 per second, are independent of the alpha rhythm, though similarly affected by the same " general excitatory conditions," tend to be inhibited by tactual stimulation, and that their relation to the sensori-motor areas is probably analogous to that of the alpha rhythm to the occipital visual association regions. This point of view seems to have more to commend it than that of Berger and Rohracher (1937), who both regard the beta rhythm as the accompaniment of psychical activity. There is, of course, no *a priori* reason why the precentral regions should not have a rhythm of their own, and undoubtedly a disproportionate amount of attention has been given to the superficial features of the occipital discharges by many workers. Jasper and Andrews also mention tentatively the appearance of even faster rhythms at about 50 per second, which they propose to call " gamma rhythms," but whose significance they do not attempt to discuss. Dietsch (1932) made a Fourier analysis of several electro-encephalograms and found many components between 10 and 50 per second. This does not, however, mean that the irregularities of the record are actually due to the existence of such components. Rohracher (1937*a*, 1938), using a similar method, states that a normal alpha rhythm has no harmonics and is therefore a pure sine wave. For reasons which are not quite clear he infers that the alpha rhythm is an expression of vegetative rather than psychical processes in the cortex. Rohracher (1935) has described frequencies up to 1,000 per second which, like the beta waves, he finds to accompany mental activity. No one else has succeeded in recording these discharges, and they must therefore be suspect, though Rohracher appears to have taken great trouble to control his experiments.

By placing the subject close to the antenna of a short-wave oscillator, Cazzamalli (1935) claims to have detected radiations with a frequency of several millions per second proceeding from the head during emotional crises and efforts of imagination. Although the experiments take place in a leaden chamber, control of the possible sources of interference does not seem to have been very thorough, and precise details of the apparatus are not forthcoming. It is possible that, if genuine, the effect might be due to variable damping of the local oscillator by the subject. At present a benevolent scepticism would seem the correct attitude to these picturesque claims.

The alpha and beta rhythms are the only discharges which can quite confidently be ascribed to the brain in healthy human subjects, but by analogy with other animals there must be other electrical phenomena. The work of Kornmüller (1937), Adrian (1933, 1936*a*, 1936*b*), Adrian and Matthews (1934*b*), Bartley (1933*a*, 1933*b et seq.*), Bartley and Bishop (1933 *et seq.*), Gerard, Marshall, and Saul (1936), Rheinberger and Jasper (1937), Marinesco, Sager, and Kreindler (1938*a*), and many others indicates that many potential rhythms can be found in the cortex of animals. The significance of these potentials and their relation to cyto-architectonic structure and function are still matters for experiment and conjecture, but it is probable that if leads were taken directly from the human cortex a similar diversity of discharge would be revealed (*cf.* Foerster

and Altenburger, 1935). With electrodes on the scalp the cortical potentials are attenuated, appearing only 1/50 to 1/100 the size of directly recorded discharges. This means that the comparatively small local " Eigenströme " would be swamped by background noise and artefacts, leaving only the largest rhythms visible in the record. There is also the possibility that the greater complexity of function of the human cortex entails less synchronization than in the case of experimental animals. The opportunities for direct recording under a local anæsthetic from normal human brains are of course very limited.

The foregoing descriptions apply to the electro-encephalogram of normal waking human subjects. Intermediate between these and the abnormal conditions which must presently be discussed is the state of *natural sleep*, most extensively studied by Loomis, Harvey, and Hobart (1937), whose special technique permits the continuous observation of a subject throughout the night. These workers find that from the electro-encephalographic standpoint there are five stages of sleep. The first, in which the subject is still conscious but feels drowsy, is characterized by normal alpha waves at the usual frequency. The second stage, which they call " floating," is the first of true sleep, and is negative in the sense that no definite rhythms can be detected. In the third stage, which may last much longer than the previous ones, intermittent bursts of waves appear at 14–15 per second. These are called " spindles." In the fourth stage there are both spindle and slow, random " delta " waves. When the author reported the location of cerebral tumours by the slow discharges produced in adjacent cortex (1936) the name " delta waves " was suggested for the abnormal rhythms. Loomis and his collaborators and most other workers have adopted this term and used it—probably quite rightly—to describe the slow waves discovered in sleep and in many other conditions. The fifth stage is characterized by an increase in size and duration of the delta waves. These observations have been confirmed by Blake and Gerard (1937).

As will be seen, the E.E.G. in the fifth stage of sleep resembles in some ways that found in certain pathological conditions. During the second stage, arousal stimuli which in the waking subject would tend to inhibit the alpha rhythm may be followed by a train of alpha waves, that is by a transient emergence from the second to the first stage. By arranging that the subject should press a key on awakening from a dream it was found that many dreams occur with a burst of alpha waves in the second stage. This facinating study is difficult to interpret, since there is so little information on other aspects of sleep.

Jasper and Andrews (1938) have found that the " spindles " are developed from the precentral beta rhythm as sleep progresses and suggest that the slower potentials are slowed alpha waves. Since there appear to be stages of electrical inactivity between the alpha-dominant first stage and the random delta fifth, this interpretation seems difficult to accept. There has been a very general tendency to describe the slow waves which occur in many abnormal conditions as " slow alpha rhythm," and certainly all the electrical manifestations of the brain may be of the same fundamental nature, but at this stage of development

it would seem more useful to reserve the term alpha rhythm for discharges between 8 and 13 per second in normal conscious subjects.

The E.E.G. in *hypnosis* has been studied by several workers. Loomis, Harvey, and Hobart (1936) found that hypnotic sleep has little electro-encephalographic resemblance to natural sleep. They found the alpha rhythm slightly slowed ; suppression of the alpha rhythm by a painful stimulus continued even when anæsthesia was suggested and no sign of pain was visible, but on the other hand, the rhythm could be stopped and started by suggestion that the subject could or could not see, provided that in the latter case the " effort to see " associated with opening the eyes was minimized by strapping the eyes open. Marinesco, Sager, and Kreindler (1937) also found a reduction in the alpha frequency. In a few unpublished experiments, Golla, Graham, and Walter found no abnormality in hypnotized subjects. In *auto-hypnosis* as practised in certain Eastern cults the author has found that the alpha rhythm may be considerably increased in size and persistence. Records taken from an Indian engaged in meditative abstraction showed an almost continuous train of normal alpha waves, which were very resistant to inhibition by external stimuli, though in the same subject shutting the eyes without meditation produced a normally irregular discharge.

Changes in the *ionic and gaseous environment* of the brain naturally affect its electrical activity, but investigation of this subject in human beings is difficult and dangerous. Voluntary hyperpnœa was found by Gibbs, Davis, and Lennox (1935) and Lennox, Gibbs, and Gibbs (1936) to produce some slow waves in normal subjects and to enhance the slow discharge already present in abnormal ones, while inhalation of CO_2 or administration of ammonium chloride reduced the tendency to produce slow waves. These effects have also been found by Golla and Walter (unpublished). It is not possible to decide whether they are due to a direct influence on the nerve-cells or to the well-known action of CO_2 as a cerebral vaso-dilator. Golla and Walter also found that the quiet period induced in an epileptic by breathing CO_2 was always followed by a reactive phase, during which bursts of large slow waves appeared, and sometimes also by a fit or fugue. This evidence seems rather in favour of the vascular theory of the action of CO_2 on the E.E.G., since a slow " overswing " is more characteristic of the blood vessels than of the blood itself. On the other hand, the phenomenon may be related to the " rebound " observed after inhibition of a spinal reflex.

The sensitivity of the E.E.G. to slight changes in the acidity of the blood has been compared by Gibbs, Gibbs, and Lennox (1938) and Gibbs (1937*a* and 1937*b*) to that of the respiratory centres to the same stimulus, and the mechanism of the response, whatever it is, may be the same in both. Three objections may be made to the comparison, however. First, that the observations which most strongly suggest the similarity have been made on abnormal subjects ; secondly, that there is no evidence that the electro-encephalographic changes are due to a direct effect on the cerebrum ; and thirdly, that the effects of changes of acidity appear to be directly opposite in the respiratory centre and the cortex ; over-ventilation, which reduces the CO_2-content of the blood and results in inactivity

of the respiratory centre and apnœa, is associated with an increase in the electrical activity of the cortex. This paradox and the other difficulties resulting from argument by analogy will be discussed later.

Changes in the *glucose concentration* of the blood are not accompanied by alteration of the E.E.G. unless they are so great as to produce profound general effects. Hypoglycæmia induced by insulin in the treatment of schizophrenia is characterized by a reduction in frequency and increase in amplitude of the alpha waves (Berger, 1937 ; Hoagland, Rubin, and Cameron, 1937 ; Marinesco, Sager, and Kreindler, 1938*b*). In deep hypoglycæmic coma, large slow waves are found. The technique of the workers responsible for these observations was not very advanced, and it is possible that the apparent change in the alpha rhythm during the early stages of hypoglycæmia is really the first sign of the slow waves found in the later stages.

The effect of *drugs* upon the E.E.G. has attracted considerable interest.

Alcohol, consumed in the customary amounts, tends to make the alpha rhythm more prominent, and in large quantities lowers the frequency (Loomis, Harvey, and Hobart, 1936). In acute alcoholic poisoning large slow waves are usually seen. In Korsakow's syndrome also Berger (1933) reports irregular slow waves with a duration of 130 to 190 milliseconds.

Administration of the volatile fat solvent *anæsthetics* produces a marked effect on the E.E.G. Berger (1929) reported an increase in frequeency during the excitation phase of chloroform anæsthesia, and in the cat the first effect of ether was found to be the production of a small high-frequency discharge (Bremer, 1936). During deep ether or chloroform narcosis large, slow, rhythmic waves appear over the whole cortex (Berger, 1929 ; Walter, 1937). The frequency of these waves is 2 to 3 per second, and their amplitude may reach several hundred microvolts. Loss of consciousness due to inhalation of nitrous oxide, carbon monoxide, or other substances resulting in anoxæmia is also accompanied by the appearance of slow waves in the E.E.G., but they are not usually as regular as those seen with ether and the other fat solvents. These slow waves are usually in phase in corresponding areas of the two hemispheres.

The effect of derivatives of barbituric acid is entirely different. For example, injection of evipan is followed by a large discharge over the whole cortex at a frequency of about 8 per second (Berger, 1933, 1934 ; Walter, 1937). This begins abruptly with the onset of unconsciousness and dies away rapidly as the subject returns to normal. The appearance of this discharge is so similar to the normal alpha rhythm that it is tempting to suppose that it is due to an interruption of the afferent pathways for sensory impulses to the cortex. Bremer (1936), arguing chiefly from the similar results which he has obtained in animals, postulates a block in the thalamus which frees the cortex from the upsetting effect of the inflow of sensations—a true anæsthesia. Barbiturates, which are more used as sedatives than as narcotics such as luminal, do not have this effect in the usual doses ; in fact, they may actually diminish the alpha rhythm.

Drugs of the *alkaloid* group do not appear to have any regular effect upon the E.E.G. in the usual doses, but Berger (1932) reports abolition of the alpha rhythm by administration of scopolamine and morphine.

Apart from the anæsthetics, the analeptic and convulsant drugs have the most dramatic effects upon the E.E.G. These have been studied in animals by Fischer (1933), Fischer and Löwenbach (1934*a* and 1934*b*), Bartley (1933*b*), Kornmüller (1937), Adrian and Matthews (1934*b*), Dusser de Barenne and McCulloch (1936*b*), and Gozzano (1936). The changes which occur in the human E.E.G. on administration of convulsants has been studied in epileptics by Lennox, Gibbs, and Gibbs (1936), and Cook and Walter (1938) have recorded and localized the large waves which precede and accompany the convulsions induced by cardiazol in the treatment of schizophrenia. These various observations will be discussed again in connection with epilepsy, but the general results may be outlined here.

1. Local application of a drug such as strychnine or thujone to an animal's cortex produces a local discharge of large waves at a frequency of 2 to 6 per second. The concentration required to produce this effect varies for different areas of the cortex. In the motor regions the local outburst of waves is accompanied by convulsive movements of the limbs concerned. The local discharge is often grouped, that is, two or three waves may appear in a fraction of a second, to be followed by a second or so of quiet before another burst of waves appears.

In certain conditions the waves may be conducted for a few centimetres from the point of application at a rate of 15 to 20 centimetres per second (Adrian and Matthews, Dusser de Barenne and McCulloch). Gozzano states that when a local discharge is produced in a given cortical region in one hemisphere the corresponding area in the opposite hemisphere also shows a discharge at the same rate which can be abolished by section of the corpus callosum.

2. Injection of a convulsant drug in man results in the appearance of waves at a frequency of about 5 per second over the whole cortex. If a convulsion follows, a sudden greater outburst occurs in the frontal region, and this spreads over the greater part of the cortex, increasing in size and decreasing in frequency as it does so (Cook and Walter).

Mescaline was found by Chweitzer, Geblewicz, and Liberson (1937) to produce two effects, first a transient augmentation and then a prolonged depression of the alpha rhythm. They also found, as did Golla, Graham, Guttmann, and Walter in some unpublished observations, that even with the eyes shut a subject with mescal hallucinations produces only a very few rather rapid alpha waves, whatever his normal degree of activity.

Drugs whose action is supposed to be related to functions of the *sympathetic* nervous system produce no definite direct effect upon the E.E.G. in normal persons. The abnormal discharges associated with " pyknolepsy " in children were found by Golla, Graham, and Walter (1937) to be abolished by administration of benzedrine sulphate in small doses, and this drug may also make the alpha rhythm less persistent in subjects whose normal rhythm is particularly prominent. This effect may be connected with the well-known arousal effect of benzedrine.

The effect of *endocrine secretions* upon the E.E.G. has not been fully investigated. Lindsley and Rubinstein (1937), Jasper (1936), and Gerard (1936)

report that administration of thyroid extract is followed by a slight increase in the alpha frequency in some cases, but the significance of this is doubtful.

In brief, the agencies which have the greatest effect upon the E.E.G. are those which are known to affect the central nervous system directly. Those affecting consciousness produce the most dramatic results, and the change usually consists of the appearance of large waves which are slow in the case of cerebral narcotics, faster in basal narcotics and convulsants.

Abnormal Conditions

The study of *nervous and mental disease* has naturally tempted the majority of workers away from a closer investigation of the normal electro-encephalogram. Berger's original intention as a neurologist and psychiatrist was to apply his methods to diagnosis, and there is scarcely a condition on which he has not reported some observations.

The possibilities of error and misinterpretation have already been emphasized, and it is unfortunate that many original discoveries reported by Berger and others who have used a single-channel technique must be given a low assessment, either because artefacts were not excluded or because observation is entangled with opinion.

When the *intra-cranial pressure* is raised by such agencies as obstruction of the ventricles, concussion, meningitis, or cerebral tumour, a slow discharge at about 3 per second is found over the whole cortex (Berger, 1930 ; Walter, 1936, 1937). The waves are often as large as 100 microvolts and may resemble in their regularity the potentials found during ether anæsthesia. In the writer's series of cases no correlation was found between the actual pressure of the cerebrospinal fluid and the degree of prominence of these slow waves, which seemed more closely connected with the extent to which cortical function was impaired. In several cases the slow diffuse discharge associated with a raised intracranial pressure was greatly reduced by intravenous injection of hypertonic solutions, but much less affected by withdrawal of fluid from the ventricles. Cases of cerebral œdema with no change in ventricular pressure also show a slow discharge, and it seems likely that the œdema is the important factor rather than the increase in hydrostatic pressure. The E.E.G. in infants with hydrocephalus is difficult to interpret, since the normal rhythm is slow in very young children.

Cases of *cerebral tumour* provide one of the most dramatic illustrations of the interest of clinical electro-encephalography. Berger (1933) reported some cases in which the E.E.G. gave signs of local abnormalities consisting either of slow waves or of an abnormal independence of the alpha rhythm on the two sides. Walter (1936, 1937) described sixteen cases in which records taken with three channels enabled a focus of delta waves to be localized to within a centimetre or so. In all cases a tumour was later found in the region of the focus. This series has now grown to over 100 cases, and the possibility of locating cerebral tumours by electro-encephalography may be considered definitely established. The general results are as follow. Confirmation of these findings has recently been supplied by Case (1938) and Case and Bucy (1938).

1. The great majority of tumours which affect the cortex either directly by

infiltration or indirectly by other means produce in it a condition in which a delta discharge occurs.

2. The new growth is entirely inactive electrically (*cf.* Foerster and Altenburger, 1935).

3. Tumours several centimetres below the surface commonly give rise to a delta discharge in the cortex directly above, which may also show some local flattening or œdema.

4. When the local electrical signs of a tumour are masked by a general delta discharge due to raised pressure, a focus may be revealed by a reduction of the pressure by osmotic means.

5. The greater and more acute the abnormality produced in the cortex, the slower are the delta waves. Meningiomata and deep, slow-growing gliomata may be associated with a discharge approaching the alpha rhythm in frequency. A meningioma which compresses the cortex may produce a discharge which is slow in the centre of the affected area and faster towards the periphery.

6. In about 3 per cent. of cases found to have a cerebral tumour, no abnormality has been noticed in the E.E.G. The tumours in these cases have been either small meningiomata or astrocytomata. A normal E.E.G. is not conclusive evidence that no tumour exists.

7. In a few cases of cerebellar tumour a delta focus has been found on the side of the tumour by leading off from just behind the mastoid process. Midbrain tumours cannot be localized and usually produce no abnormality except by raising the intracranial pressure. Griffiths, Nevin, and Walter (to be published) found a very large regular general delta discharge in a comatose case of hypothalamic tumour in which the pressure was normal. The E.E.G. resembled that found in deep sleep, and may possibly be due to destruction of a " waking centre " in the hypothalamus.

Circulatory disorders are not usually associated with change in the E.E.G. Even the most severe cases of arteriosclerosis present no abnormality, and *cerebral hæmorrhage* and *thrombosis* are not detectable except for a short period immediately following the catastrophe (Berger, 1931 ; Walter, 1936). Berger has reported one case of aphasia following thrombosis in which the beta rhythm was more prominent than normal and declined as the condition improved. It can only be supposed that in cases of cerebral arterio-sclerosis the symptoms are due to a general depression of the cortex, no part of which is sufficiently affected to give rise to a delta discharge.

Injury to the cranial contents has not been studied extensively. Deliberate surgical trauma produces a transient local delta discharge which passes off in about a week. This would probably be found also in cases of accidental injury, but in the recovery stages nothing definite has been reported.

Diseases of the *Meninges* are sometimes associated with a general delta discharge. Delta foci have been found by the author in a few cases of localized *Arachnoiditis* and these may sometimes mimic cerebral tumours very closely. In two cases there was a delta discharge from both frontal poles which declined as the clinical condition improved.

Infections of the central nervous system are associated with electro-encephalo-

graphic abnormalities chiefly when the cerebral cortex is directly affected. *Cerebral abscesses* may be located in the same way as cerebral tumours, and some types of encephalitis appear to be associated with a general delta discharge. The E.E.G. in *Encephalitis lethargica* was found to be normal in the resting stage by Berger (1931, 1933), but Jasper (1936) found slight abnormalities in a few cases. A mesencephalic lesion would not, of course, be expected to produce a very definite change in the cortical E.E.G. (Jasper, 1936*b*, found no abnormality in two cases of *Paralysis agitans*.) Indefinite abnormalities have been reported (*e.g.* Berger, 1931) in cases of *disseminated sclerosis* and *general paresis*, but there has been no satisfactory confirmation of these findings, and the position is uncertain also with regard to *encephalomyelitis* and *poliomyelitis*.

Disorders of voluntary movement, such as *torsion spasm*, *chorea*, and *athetosis*, do not seem to be associated with abnormalities in the E.E.G., and recording is very difficult if the movements are violent. Negative evidence of this sort is not conclusive, but it would suggest that the movements in these conditions are not cortical in origin.

Congenital disabilities, such as hemiplegias and diplegias, do not present abnormalities unless the cortex is affected, and then only apparently in such cases as suffer also from convulsions. This is probably an illustration of the general truth that a definitely abnormal E.E.G. is found only when the cortex is in some intermediate stage of degeneration and not when it is completely atrophied. Thus, in degenerative diseases such as *Alzheimer's disease* abnormalities may be found, but they are not necessarily greater in the terminal stages (*cf.* Berger, 1931).

Intoxications of the cerebral hemispheres have been considered already in relation to narcotics. Jasper and Andrews (1936) describe irregular slow waves in cases of lead encephalitis, and this sort of discharge is characteristic of all sorts of conditions in which the hemispheres are poisoned : the degree of electro-encephalographic abnormality is an indication of the extent and severity of the intoxication rather than of the nature of the poison. The fact that, particularly in the case of anæsthetics, the condition is reversible, indicates that a prominent delta discharge is produced by cortex in a state when no permanent damage has been done. It has been observed, moreover, that intoxication may go beyond the delta stage, and that then recovery is impossible or at best incomplete.

The group of *paroxysmal and convulsive* disorders is of unique interest from the electrical standpoint. The mystery which surrounds the nature and origin of the epilepsies is as humiliating to the physiologist as it is exasperating to the clinician, but there is reason to hope that the spell may eventually be broken with the help of electro-encephalography.

In some of his quite early papers Berger (1931, 1933) reported a large, slow discharge in cases of epilepsy complicated by dementia or feeble-mindedness, and he showed also that a minor attack is accompanied by very large waves at about 3 per second, while during the period after a fit the E.E.G. is remarkably quiet. These observations have been confirmed and extended by several workers. The E.E.G. during seizures has been studied in great detail by Gibbs,

Gibbs, and Lennox (since 1935) and they have recently presented a useful summary and interpretation of their results obtained by multiple recording from over 400 patients (1938 *a* and *b*). Their conclusions are as follow :

" 1. Seizures involving the cortex are accompanied by distinct and characteristic fluctuations in the action potentials of the brain.

" 2. The rhythm which obtains during seizures is distinctive for the three main types : *grand mal* has a fast, psychomotor attacks (psychic variants) a slow, and *petit mal* an alternating fast and slow rhythm. The exact pattern of the seizure tends to be characteristic for each patient.

" 3. Antecedent to these gross abnormalities of rhythm is the lack, in epileptics, of a competent control of cerebral rhythms.

" 4. Some patients have sub-clinical seizures which are typical short disturbances of rhythm, not attended by subjective or objective evidence of a seizure. *Petit mal* may occur during sleep.

" 5. There is evidence that *grand mal* may be predicted many hours in advance.

" 6. In some patients abnormal activity begins in one area of the cortex and spreads to involve other areas. . . ."

Gibbs, Gibbs, and Lennox also suggest that sedatives are more effective in *grand mal* than in *petit mal* because they slow the cortical rhythms, while the *petit mal* rhythms may be temporarily abolished by a rise in the CO_2 tension or glucose concentration of the blood.

Some amelioration was produced in two cases out of three in whom a frontal lobectomy was performed on the basis of abnormalities in the E.E.G.

These observations suggest to Gibbs and his associates that epilepsy is a " Paroxysmal cerebral dysrhythmia."

The electro-encephalogram is often abnormal between seizures also. Golla, Graham, and Walter (1937) found that out of 214 cases of epilepsy, 91 showed a definite abnormality in the E.E.G. between fits. These observations have been continued and the number of cases examined is now approaching 1,000. It would seem that of all patients under 40 years old who complain of fits, about 50 per cent. show some abnormality in the E.E.G., and of these the majority are cases of idiopathic *grand mal*. For some reason few patients over the age of 40 show any abnormality, whatever the diagnosis, and the disappearance of the discharge at about that age has been watched in a few cases, in whom, however, the fits continued. In most abnormal cases the discharge resembles that found in cases of cerebral tumour, and may accordingly be described as a delta discharge ; it is not often more than 1/10 the size of the smallest seizure waves. The focus can usually be located by three-channel recording, and in cases of *grand mal* is most often in the region of the superior frontal gyrus on either or both sides. In cases complaining only of minor attacks the focus is usually post-central, and in the so-called pyknolepsy of children is in the occipital poles. The position of the focus appears to have some connection also with the character of the attack in *petit mal*, though not with the nature of the aura in *grand mal*. When a patient has a fit during examination the seizure waves can be seen to start as an increase in the focal

resting discharge which spreads, often quite suddenly, to involve other parts of the cortex, becoming at the same time larger, slower, and more regular. The " subclinical seizures " of Gibbs and his co-workers can be recognized in cases of *petit mal* as a period of less pronounced augmentation and expansion of the resting delta discharge.

The resting delta activity may be restricted but not diminished by drugs effective in controlling fits, although in some cases of pyknolepsy the fits and the focus have both disappeared during administration of benzedrine sulphate. There are, however, spontaneous fluctuations in the size of the discharge and these are correlated with changes in the frequency of the fits.

There is evidence that the cortical area responsible for the delta discharge also shows slight but definite histological abnormalities. In some cases the delta focus was associated with gross atrophy.

From the clinical point of view it is important that cases of traumatic epilepsy do not show a resting abnormal focus, though the seizure waves in these cases are the same as those in idiopathic epilepsy. Cases diagnosed as hysteria show no abnormality, either between or during fits, except when the attack is accompanied by voluntary hyperpnœa. These facts make possible the differential diagnosis of idiopathic and other types of epilepsy, though only positive results are completely trustworthy, since a certain proportion of idiopathic epileptics give normal records.

These observations and those of Gibbs and his colleagues fit together admirably, and the whole forms an imposing addition to the facts about epilepsy, but the data are very much harder to integrate than they are to collect. Jasper and Hawke (1938) have recently published work confirming these observations. There is no doubt that in most cases of idiopathic epilepsy a part of the cortex is in an electrically abnormal condition, and that when a fit occurs this abnormality is enormously increased. There is, however, no proof that the electrical phenomena indicate a truly cortical origin for the condition preceding and accompanying the epileptic symptoms. The results of cortical excision are not promising from the therapeutic standpoint, and the failure to stop fits by enlightened surgical intervention suggests that the cortical manifestations may have only a secondary association with the true cause of epilepsy. Golla, McKissock, and Walter (to be published) found that the excision of a delta focus in epileptics was followed by a few months of comparative freedom from fits, but the patients slowly returned to the pre-operative condition. The treatment seemed no more effective than any other major operation.

The importance of the information obtained about epilepsy by electroencephalography lies first in its use in empirical diagnosis and secondly in its value as a stimulant to the experimenter. For example, the frequency with which delta foci are found in the superior frontal gyrus in idiopathic major epilepsy and the fact that convulsions induced by cardiazol (Cook and Walter, 1938) are associated with a high-potential electrical discharge in the same region suggest that this area of the cortex has something to do with convulsive movements. In general, a delta discharge indicates inactivity of the area concerned, and if this is true also in epilepsy, it might be argued that integrity of the pre-

frontal area is essential for the control of voluntary movements and the prevention of convulsions. This hypothesis accounts for the therapeutic ineffectiveness of removal of this area and suggests that much remains to be learned about its function and connections.

The E.E.G. in *narcolepsy* usually shows little definite abnormality, but there is often a very prominent alpha rhythm from a large focus, and the same has been found in some cases of *cataplexy*. The alpha rhythm becomes normal when the sleepiness is controlled by benzedrine (Walter, unpublished). No definite abnormality has been reported in cases of *migraine* or *vaso-vagal attacks*. In one case at first diagnosed as *myoclonus* and later as *epilepsia partialis continua*, the author found a large discharge from the right superior frontal gyrus in rhythm with involuntary movements of the left side of the body. The discharge resembled that found during the clonic stage of a fit, but involved only a comparatively small area, and this patient had never had a general seizure of any sort. This is further evidence for the connection between frontal areas and involuntary movements, but the temporal relation between the cortical discharge and the action potentials of the affected muscles was not constant (*cf.* Jasper and Andrews, 1938, and Travis and Cofer, 1937). The movements in this case resembled a *tic*, but in cases of true *tic* no abnormality is found.

The *neuroses* have so far proved a sterile field for electro-encephalography. The alpha rhythm reflects to some extent changes in the mood of a subject and seems particularly sensitive to fluctuations in his attention, but a highly neurotic individual usually gives a normal record. Exceptions are sometimes found in " problem " children, who may give records similar to those of epileptics. Solomon, Jasper, and Bradley (Jasper, 1937) found a correlation between the degree of abnormality of the patients' behaviour and the abnormality of the record, both in different patients and in the same patient from time to time. In the author's experience such children are actually suffering from an almost continuous series of *petit mal* attacks and usually develop true epilepsy later (except in cases of pyknolepsy which clear up spontaneously). In these cases electro-encephalography has been found useful as an aid to diagnosis and prognosis. After a painstaking survey, Travis and Knott (1936) have shown that the E.E.G. in *stutterers* is not significantly abnormal.

The E.E.G. in the *psychoses* has been studied by Berger (1931, 1933*a*, 1933*b*, 1937*a*, 1937*b*, 1938). Lemere (1936), Travis and Malamud (1937), none of whom report any definite abnormality in schizophrenia or manic-depressive psychoses. Berger (1937*b*) emphasizes the frequency of artefacts when leading from insane patients and concentrates on the E.E.G. during hypoglycæmic shock treatment. Lemere considers that schizophrenic patients usually have a poor alpha rhythm as compared with normals or manic-depressives. Hoagland, Rubin, and Cameron (1936, 1937*a*, 1937*b*, 1938) claim that a significant proportion of schizophrenics give slow swings of the base-line which they propose to class as delta waves. They have devised a measure of the incidence of these delta waves in a record, which they call the " delta index " and state that this is significantly higher in untreated schizophrenics than in normal subjects, and that the index in schizophrenics drops during treatment or spontaneous remis-

sion. MacMahon and Walter (1938) have followed up this question and find that there is indeed a certain amount of slow random activity in some types of schizophrenia, but suggest that many of the large waves to which Hoagland and his collaborators attach importance are in reality due to eye-movements, which are particularly common in this class of disorder, and moreover diminish with clinical improvement. MacMahon and Walter also find a different sort of abnormality ; an alpha rhythm which persists during all forms of visual and mental activity. This was found in patients with symptoms of volitional weakness, and they suggest that a perpetual alpha discharge may be associated with the patient's inability to mobilize his sensory resources or to relate afferent impressions to internal associations.

It is clear from what has already been done that interpreting the E.E.G. in psychoses will be a difficult and controversial problem, made still harder by the uncertainties of clinical diagnosis. In no other branch of electro-encephalography is greater vigilance required to escape the three enemies of precision—artefacts, statistics, and analogies ; and in no other branch are the rewards to be gained by clinical application so tempting and so meretricious.

The foregoing survey of facts must now be still further condensed into compact generalizations. The most obvious one is that the chief sign of cortical abnormality is the appearance of slow delta waves, and as an empirical guide to interpretation the presence in a record from a waking adult subject of discharges at a frequency of less than 7 per second may be taken as definitely pathognomonic. In children the normal limit is lower. The other criterion of abnormality is the persistence of a seemingly normal rhythm through all stages of activity and attentiveness.

We do not know how or why delta waves are produced, but it seems most likely that they represent a true change in the natural electrical period of the cortical neurones, a change which is usually ominous but yet reversible if the cause is removed. During delta activity no useful work can be done by the neurones concerned. Sometimes the delta waves are so large that we may suspect them of paralysing the cortex by electrocution, as it were, and we may speculate as to whether this may not be their special function in certain conditions, just as the function of pain is sometimes to immobilize an injured part. In order to explain the occasional great size of the slow waves it may be necessary to invoke a series connection for the cortical cells, similar to that evolved from muscle cells in electric fish. The rhythmicity of the discharge need cause no wonderment, but nor should it be taken as an excuse for free speculation. Parables and analogies are valuable stimulants but bad food for thought, and the fact that a terminology designed to classify phenomena observed in simpler systems can be used to describe certain features in the behaviour of the central nervous system proves nothing except that it can be so used. Nevertheless one phase of scientific reasoning permits description of the new in terms of the old, and if we look for something in simpler tissues that will help us to understand the normal and abnormal electrical rhythms of the brain, the phenomena which seem most likely to be not merely similar but homologous are the slow electrotonic potentials of the spinal grey matter described in detail by Barron and

Matthews (1935, 1938). A discharge of impulses from a spinal neurone is accompanied by a slow potential swing similar in its time relations to the cortical rhythms, and altogether different in form from the action potentials of peripheral nerve. Moreover, a discharge of impulses may be evoked by a small externally applied current in the right sense, and reversal of this current inhibits the discharge. There is also evidence that such slow electrotonic potentials produced by nerve cells may influence conduction even in fibres to which they are not directly connected. These observations of Barron and Matthews suggest the possibility of translating Sherrington's " C.E.S." and " C.I.S." into terms of katelectrotonus and anelectrotonus in the grey matter, and since the cortex contains chiefly grey matter it would not be altogether fantastic to suppose that the E.E.G. is a record of rhythmic cortical alternations of kat- and anelectrotonus rather than of cortical action potentials, a term which should probably be restricted to the electrical features of a propagated disturbance. It can easily be understood that in normal circumstances the frequency at which a cell in the cortex can produce electrotonic alternations will be fixed within narrow limits by the physical dimensions of the oscillating system and that when a certain number of cells oscillate in synchrony the potentials will be detectable as an alpha or beta rhythm. The apparent size of the rhythms will depend upon the number of cells beating together, and this agrees with the practical observation that a high-potential rhythm indicates a large focus. The normal rhythms are associated with some degree of inactivity in the cortex, and it seems probable, therefore, that the less the activity of a part of the cortex, the greater the degree of synchronization of the cells concerned, but it is not certain whether the electrical quiet associated with cortical activity is due merely to desynchronization of cells which are still oscillating at their natural frequency, or whether the discharges of each cell are damped. The former explanation seems the more probable.

Returning to the discharges in abnormal conditions we may suppose that a focal disturbance such as a neoplasm results in a reduction of the natural period of the cells in its neighbourhood and that their discharges are synchronized in the same way as the normal ones. Dusser de Barenne and McCulloch (1936*a*) have shown that laminar coagulation of the upper layers of the cortex abolishes the local characteristic currents and leaves a delta-like discharge which they presume emanates from the lower layers. The origin of the delta-foci in epileptics remains a subject for speculation. The change in time relations of the affected area may account in part for its inability to participate in normal activities, which may require some sort of isochronism of several areas or levels. The disappearance of characteristic local discharges in narcosis and their supersession by a general slow discharge has been studied in animals by Drohocki (1938), who refers to this state as the " Echostadium." It is remarkable that in man whenever consciousness is lost the normal local rhythms vanish and are replaced by a much larger, slow, general discharge, and that a similar delta rhythm appears locally when only a part of the cortex is affected, though the first signs of interference may be slowing, persistence, or irregularity of the normal resting discharges if any are detectable.

Electro-encephalography has developed as a technique rather than as a science, but since the phenomena have turned out less like others than was expected, fresh theories must eventually arise. At present the sorting and classification of data is only beginning and there must be many facts still to be discovered. Meanwhile, as interpretation becomes more confident and more detailed, the usefulness of electro-encephalography will increase, and we may hope that in time a precise neurophysiology will develop from the marriage of electro-physiology and clinical neurology.

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Ophthalmo-Neuromyelitis, multiple und diffuse Skelerose bei Ost-Asiaten in Niederl. Ost-Indien. (Neuropticomyelitis, multiple and diffuse sclerosis in Eastern people in the Dutch East Indies.) W. J. C. Verhaart. 93.

Nerve Lesion in Anæmia.—In four cases of pernicious anæmia examined post mortem, Weigert-Pal sections of peripheral nerves showed evidence of degeneration. (E. A. C.)

ALLGEMEINE ZEITSCHRIFT FÜR PSYCHIATRIE UND IHRE GRENZGEBIETE

Vol. 108. No. 1. 1938.

Aufgaben und Grenzen von Gesetzgebung, Rechtsprechung und Heilkunde, erörtert an den Beziehungen zwischen Eheanfechtung, Erbkrankeits und Ehegesundheitgesetz. (Medico-legal aspects of marriage and sterilization.) F. Neukamp. 3.

Die Eltern der Hilfsschulkinder. (The parents of backward children.) W. Busse. 42.

Über Dauerschäden nach Hirntrauma bei Kindern und Jugendlichen. (Permanent lesions following cerebral trauma during childhood and youth.) F. Faust. 72.

*Die traumatische Epilepsie, unter besonderer Berücksichtigung der an der Psychiatrischen und Nervenklinik zu Jena in den Jahren von 1920–1935 behandelten Fälle. (Cases of traumatic epilepsy admitted to the Jena Mental and Neurological Hospital from 1920 to 1935.) W. Seydel. 94.

*Disposition und Belastung zur Progressiven Paralyse. (Hereditary disposition to G.P.I.) A. Stegmann. 115.

Über Körpergewichtsstudien bei insulinbehandelten Schizophrenen. (Body weight during insulin treatment of schizophrenia.) A. v. Braunmühl. 144.

Über einen Fall spätenzephalitischer Seelenstörung mit epileptoiden Erscheinungen und liliputiformen Halluzinationen. (A case of post-encephalitic psychosis with epileptiform and hallucinatory symptoms.) J. Hühnerfeld. 157.

Die Breite Wiese bei Lüneburg. Ein Betrag zur Kenntnis der Irrenpflege in Niedersachsen vom 16 bis 18 Jahrhundert. (The Breite Wiese Mental Hospital. Psychiatric treatment in the 16th–18th centuries in Lower Saxony.)

Traumatic Epilepsy.—The total number of patients with traumatic epilepsy within 15 years was 250. In 76 per cent. there was a severe trauma with fracture of the skull and coarse lesions of the brain. The free interval between trauma and first attack was on the average 2 years 7 months. In the 102 cases from the war (gun-shot, shell) the interval was even larger, with an average of 3½ years; 30 out of the total number had only epileptic equivalents; in 21 per cent. the attacks were of Jacksonian type; 40 per cent. showed definite psychological changes; 6 per cent. developed a true dementia. (K. S.)

Hereditary Predisposition to G.P.I.—In 88·3 per cent. of 206 male patients and in 92·1 per cent. of 64 female patients there was a higher percentage of psychoses in the family than in the average population. The majority of the patients showed traces of mental abnormality before the time of the luetic infection. (K. S.)

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Paresis. An Analysis of 511 Treated Cases. R. A. Matthews, R. S. Brookhammer, and W. H. Izlar. 1,259.

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*Clinicopathological Considerations for Differential Diagnosis between Juvenile Paresis and Other Forms of Encephalitis. A. Ferraro, S. E. Barrera, and H. S. Gregory. 1,291.

Abstract of "One Hundred Years of Non-Restraint." E. Messinger and M. A. Amdur. 1,307.

The Pharmacological Shock Treatment of Chronic Schizophrenia. I. Murray-Rossman and W. B. Cline. 1,323.
Observations in the Hypoglycæmic Treatment of 55 Cases of Schizophrenia. D. Russlander. 1,337.
Treatment of Psychosis with Pentamethylentetrazol. H. H. Goldstein, E. F. Dombrowski, J. V. Edlin, A. P. Bay, C. I. McCorry, and J. Weinberg. 1,347.
*Blood Chemical Changes Occurring in the Treatment of Psychogenic Mental Disorders by Metrazol Convulsions. S. Maurer, H. O. Wiles, C. M. Marberg, B. Skorodin, and M. L. Fisher. 1,355.
*Rabies Vaccine in the Treatment of Epilepsy. Isidore Finkelman, A. J. Arieff, and A. Schiller. 1,363.
*The Use of Intravenous Methylene Blue in Status Convulsivus. L. Kajdi and C. V. Taylor. 1,369.
Statistical Contributions from the Mental Hygiene Study of the Eastern Health District of Baltimore. II. Psychosis in the Eastern Health District. B. M. Cohen and R. E. Fairbank. 1,377.
The Organic Background of Obsessions and Compulsions. P. Schilder. 1,397.
The Psychoanalytic Clarification of Personality Types. E. E. Hadley. 1,417.
Psychoanalytic Contributions to the Conception of Disorder Types. N. L. Blitzsten. 1,431.
The Psychology of the Swindler. W. Bromberg and S. Keiser. 1,441.
Parotid Gland Secretions in Manic-Depressive Patients. E. L. Strongin and L. E. Hinsie. 1,459.

Juvenile Paresis and Other Forms of Encephalitis.—A case is described of a nine-year-old boy presenting a syndrome indicating general involvement of the C.N.S. and progressing with a febrile reaction to a fatal termination within a few months. The pathological process involved predominantly the smaller blood vessels of the cortex, the ganglion cells, and the microglia. The blood-vessel changes showed perivascular infiltration with round cells and plasma. The nerve-cell changes varied from slight swelling to acute cytolysis. The microglial changes included formation of rod cells and numerous nodules distributed through the entire nervous system including the spinal cord. On the basis of the rapidly progressive course, the negative serological findings, the presence of numerous nodules throughout the nervous system, a diagnosis of juvenile tabo-paresis was considered unjustified. A diagnosis of acute polioencephalitis was given.

Mental Disorders and Metrazol Convulsions.—A series of determinations of *p*H, lactic acid, glucose, CO_2, phosphorus, calcium, and chloride was obtained in nine patients who were being treated by metrazol convulsions. Blood samples were drawn at varying intervals during the convulsions. At the onset the findings indicate lowering of the *p*H during active tonic convulsions. The maximum decrease of *p*H occurs from 2 to 4 minutes after the metrazol injection. The *p*H returns to the pre-injection level after about 20 minutes. In some patients there is an over-compensation of the acidosis, so that the blood becomes more alkaline. Within 3 minutes after the injection, the blood lactic acid reaches a value of 100 mg. per cent. or more and continues to rise. In one case it reached 160 mg. per cent. in 16 minutes. After 15–20 minutes it decreases, reaching normal in 45–60 minutes. After the tonic convulsions are over and clonic convulsions are proceeding, the conversion of lactic acid to glucose goes on rapidly and the blood glucose increases. The maximum attained at the end of the clonic stage was 206 mg. per cent. The CO_2 values during the convulsive stage decrease owing to hyperventilation. The inorganic phosphorus of the serum shows an increase during the convulsions. The calcium values remain within normal limits during the fits. The blood chlorides also remain within the normal range.

Rabies Vaccine in Epilepsy.—An attempt is made to verify the claims of Nikitin that epilepsy is beneficially affected by anti-rabic treatment. Thirteen patients suffering from epilepsy received a course of 21 doses administered daily. The vaccine was prepared by the Semple method. None of the patients became free from fits for any length of time, and there was no change in the frequency or severity of the attacks as a result of the anti-rabic therapy in 12 cases; the attacks ceased, however, for 2 months in one patient.

Intravenous Methylene Blue in Status Convulsions.—Many writers have reported favourably on the intravenous use of methylene blue in cases of poisoning by cyanide and carbon monoxide. These results might suggest that methylene blue could be used to combat anoxia in the C.N.S. The authors have attempted to apply this treatment to the anoxemia which is alleged to occur in the C.N.S. in status convulsivus. Only those cases where the patient was completely unconscious between the attacks were accepted as being status. Twenty-two such cases of status were treated by intravenous injection of 1 per cent. methylene blue, the volume injected ranging between 2–20 c.c. It is claimed that the injection was followed by a rapid restoration to consciousness in 13 patients (59 per cent.), and rapid complete control of convulsions in 13 (59 per cent.), and a 66 per cent. reduction of status mortality in a chronic epileptic group.

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*Relation between Precipitating Situation and Outcome in Manic-Depressive Psychosis. R. C. Hunt. 65.
The Symptoms and Treatment of Barbiturate Intoxication and Psychosis. F. J. Curran. 73.
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Eighteen Hundred and Seventeen Cases of Suicidal Attempt. A Preliminary Statistical Survey. P. Piker. 97.
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An Evaluation of Hydrotherapy in the Treatment of Delirium Tremens. R. M. Bell and P. C. Talkington. 161.
*A Comparative Study of Negro and White Admissions to the Psychiatric Pavilion of the Cincinnati General Hospital. P. S. Wagner. 167.
The Morbidity Incidence of Degenerative Somatic Diseases in Psychotics in Comparison with the Same Type of Disease in Comparable Age Groups in Civil Life. F. S. Caprio. 185.
Mental Changes in Chorea Minor. D. Shaksan. 193.
*Results of Non-Specific Treatment in Dementia Præcox. C. O. Cheney and P. H. Drewry. 203.
The People *versus* Robert Irwin, Charged with the Murder of Three Persons. 219.

Auditory Apparatus in Auditory Hallucinations.—Patients experiencing auditory hallucinations have been known to have disorders of the auditory apparatus. The purpose of this study is to determine the incidence, nature, and possible causes of these disturbances. A hundred cases were studied. The clinical material was unselected except for the requirements that the patient had suffered from auditory hallucinations recently. The series included 62 males and 38 females, ranging in age from 14 to 58 years. The auditory apparatus was carefully examined. Thirty-one patients were found to have an impairment of hearing, 19 cases of toxic deafness, and 2 of nerve deafness. Of the 19 cases of toxic deafness, 18 patients gave a history of a definite toxic factor, 16 alcoholism, 1 drug addiction, 1 toxæmia with a septic infection of the throat. No evidence of auditory hyperæsthesia was noted. Some of the cases experienced hallucinations only in one ear, but the monaural hallucinations did not bear a constant relation to the deafness of the respective ears.

Precipitating Situation in Manic-Depressive Psychosis.—The author accepts the view of Rosanow as to the ætiology of manic-depressive psychosis. He agrees that the bulk of the cases occur on an hereditary basis either under ordinary conditions of life or under the influence of external factors which are for the most part of psychogenic nature. The possibility of influencing the course of psychosis by therapy aimed at relieving the environmental stress is still a question of some practical importance. In order to study this problem the clinical records of 105 cases of manic-depressive psychosis are analysed. Of these cases 67 did not experience a serious precipitating situation, 15 had a serious situation which was relieved, and 23 had a serious situation which was not relieved. In the group without a serious precipitating situation 73 per cent. recovered with an average duration of 9·8 months. In the group with a serious situation which was relieved all recovered with an average duration of 9·4 months, but recovery did not always coincide with the time at which the situation was relieved. In the group with a serious situation which was not relieved 74 per cent. recovered with an average duration of 18·8 months.

Negro and White Admissions to Cincinnati General Hospital.—A survey of such data as are available gives no support to the view that any innate hereditary difference exists between the negro and the white man with respect to his mentality, his instinctive expression, his potential adaptability. The present study is undertaken to discover whether the behaviour in psychopathic states, including the extremes of instinctive expression, and the disruption of the personality indicate the existence of modes of reaction peculiar to the coloured man. The analysis of a year's admissions to the Psychiatric Pavilion of the Cincinnati General Hospital corroborates the observations of Malzburg, who found the total annual incidence of psychosis among negroes in New York City to be about twice that among the white population. The individual clinical records of negroes suffering from psychoses indicate no characteristic types of psychotic behaviour. The authors consider that the preponderance of psychoses among negroes is probably of environmental origin, though they adduce little evidence in support of this conclusion.

Non-Specific Treatment in Dementia Præcox.—Five hundred cases of dementia præcox were studied at a private hospital where the patients were offered facilities for intensive treatment which the majority of psychiatric hospitals did not find it possible to provide. The results are classified as regarding much improved, improved, and unimproved, and are offered as a basis for comparison with those obtained by specific treatments such as the insulin and cardiazol methods. In order to provide a reasonably long period of observation, no patients admitted since 31st December, 1935, were included. Some of the 500 patients had a course of observation of 12 years and none less than 2 years. The general conclusions from the tables given would show that in a hospital giving intensive individual care and treatment it might be expected that at the end of their hospital residence 16 per cent. of the total number of cases will be improved, 14 per cent. much improved, and 7 per cent.

recovered. Of the catatonic patients, 13 per cent. will be improved, 19 per cent. much improved, and 10 per cent. recovered. Of the paranoid cases, 15 per cent. improved, 10 per cent. much improved, and 4 per cent. recovered. Of the hebephrenics, 26 per cent. improved, 10 per cent. much improved, and 2 per cent. recovered. In simple deterioration, 23 per cent. will be improved, 13 per cent. much improved, and none recovered. If the patients have shown symptoms for not more than 6 years before admission, half of them will be benefited and 10 per cent. will recover.

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A Theoretical Field-Analysis of Automobile-Driving. J. J. Gibson and L. E. Crooks. 453.
A Qualitative Study of the Eye Movements of Good Readers. R. Y. Walker. 472.
A Comparison of Color-Blind Tests. B. R. Philip. 482.
Binocular Depth Contrast and the Conditions of the Binocular Field. H. Werner. 489.
Conditioned Discrimination : The Effect of Knowledge of Stimulus-Relationships. E. R. Hilgard, R. K. Campbell, and W. N. Sears. 498.
Variability in the Affective Judgment. W. A. Hunt and J. Flannery. 507.
Some Factors in Size-Constancy. N. M. Locke. 514.
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Effect of Stimulus-Texture upon Apparent Warmth and Affective Value of Colors. M. A. Tinker. 532.
The Pitch of a Combination of Tones. P. R. Farnsworth. 536.
The Effect of Light-Flashes During the Course of Dark Adaptation. L. K. Allen and K. M. Dallenbach. 540.

ANNALES MÉDICO-PSYCHOLOGIQUES

Vol. 1. No. 4. April 1938.

Étude Systématique de la Circulation Rétinienne chez un Groupe de Déments Séniles ou Pré-Séniles. (A systematic study of the retinal circulation in a group of senile and pre-senile dements.) Bargues, Corcelle, and Berthon. 433.
*Des Ulcérations Gastriques chez les Aliénés. (Considerées comme l'une des Causes du Refus de Nourriture.) (Gastric ulcers in the insane. Considered as one of the causes of refusal of food.) J. Dretler. 451.
*À Propos de l'Hygiene Mentale. (Quelques Reflexions.) (Some considerations on mental hygiene.) Minkowski. 467.

Proceedings of the Société Médico-Psychologique.

L'Enseignement de Mangan a l'Asile Clinique St. Anne. Quelques Souvenirs. (The teaching of Mangan at the St. Anne's Clinic. A few souvenirs.) A. Fillassier. 487.
Scotoma avec Hallucinations Lilliputiennes d'Origine Épileptique. (Scotoma with lilliputian hallucinations of epileptic origin.) Laignel-Lavastine and Mignot. 491.
Les Psychoses Intermédiaires entre la Démence Précoce et la Psychose Maniaque Dépressive. (Intermediary psychoses between dementia præcox and manic depression.) P. Chatagnon, P. Scherrer, and Mlle. Chatagnon. 494.

Gastric Ulcers in the Insane.—A clinical history of 10 cases of insanity is given. These cases had a common symptom in the refusal to take food. All were found post mortem to have ulcerative lesions of the gastric mucosa. All the 10 cases showed more or less pronounced vascular lesions in the floor of the third ventricle. Five of the cases appear to have been schizophrenics, three were general paralytics, and two were arteriosclerotic dements.

Retinal Circulation in Senile and Pre-Senile Dements.—Basing their conclusions on the experimental evidence furnished by Lambert and later by Riser, Coriadeau, and Meriel, the authors assume that the arteries of both the retina and the cortical meninges have identical vasomotor reactions, although they both differ from the peripheral vascular reactions. They proceeded to investigate the retinal circulation in cases of mental disorder due to vascular lesions. They examined the retinal vessels in 25 cases of arteriosclerotic dementia. All these cases had lesions of an atheromatous type in the retinal vessels. Thirteen patients suffering from senile parenchymatous dementia had a normal fundus oculi in nine cases. The vascular abnormalities in the other four cases were attributable to age and general physical conditions. There is evidence of a parallelism between the state of the retinal vessels and those of the meninges in arteriosclerotic dementia.

Vol. 1. No. 5. May 1938.

Des Modifications qui Pourraient Être Apporteés a la Loi du 30 Juin, 1838. (Modifications which could be made with regard to the law of 30th June, 1838.) J. Hamel and J. Lauzier. 561.
Lacunes de la Loi de 1838 en Cas d'Évasion. (Deficiency of the Law of 1838 in the case of evàsion.) J. Picard. 571.
Histoire des Projets de Révision de la Loi du 30th June, 1838. (A review of the plans for revision of the law of 30th June, 1838.) M. Desruelles. 585.

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Syndrome Préfrontal au Cours d'une Psychose Hallucinatoire Chronique. Hémorragies Méningées puis Hémorragie Ventriculaire Terminale. Étude Anatomoclinique. (Prefrontal syndrome in a case of chronic hallucinatory psychosis. Meningeal hæmorrhage followed by terminal ventricular hæmorrhage. Anatomoclinical study.) P. Chatagnon, P. Scherer, and Mlle. C. Chatagnon. 624.

Le Centénaire de la Loi du 30 Juin 1838 sur les Aliénés. Éloge de la Loi. (The Centenary of the law of 30th June, 1838, regarding the insane. Commendation of the law.) A. Fillassier. 639.

La Protection des Biens des Malades dans la Loi de 1838. (The protection of property of patients according to the law of 1838.) X. Abély. 655.

La Loi de 1838 et les Enfants. (The law of 1838 and the children.) T. Simon. 665.

L'Ésprit des Projets de Revision de la Loi du 30 Juin 1838. (The outlines of the plan for the revision of the law of 30th June, 1838.) M. Desruelles. 667.

Un Demi-siècle d'Assistance des Aliénés avant la Loi de 1838. (Half a century of assistance of the insane before the law of 1838.) P. Carrette. 674.

Vol. 1. No. 6. June 1938.

*La Rôle de la Syphilis dans la Génèse de Certains Syndromes Psychopathiques de l'Adulte. (Formes Frustes de la Syphilis Cérébrale.) (The rôle of syphilis in the genesis of certain psychopathic syndromes in the adult. Abortive forms of cerebral syphilis.) J. Dublineau. 1.

Nouvelle Note Relative aux Psychoses Grippales. (A new observation on post-influenzal psychosis.) I. Urechia. 22.

*Une Forme de Glossolalie. (Glossolalie par Suppression Littérale.) (A form of glossolalia. Consisting of suppression of words.) G. Tuelie. 31.

Proceedings of the Société Médico-Psychologique.

Action Favorable d'une Infection Rigue. (Ostéomyélite du Maxillaire Inférieur) sur und Démence Précoce Évoluant depuis Cinq Ans. (Favourable influence of an acute infection of ostéomyélitis of the lower jaw in the case of a patient suffering from dementia præcox for five years.) G. Demay and J. Naudascher. 52.

Syndrome Aphaso-Agnosto-Apraxique et Troubles Démentiels. (Aphasia-agnostia-apraxia syndrome in a case of dementia.) J. Fretet and J. Carrier. 58.

Guérison et Réembauchage des Psychopathes. (The problem of re-employment of cured psychopaths.) P. Courbon and J. Asued. 64.

La Phonopsychographie. ("Psychophonography.") P. Courbon. 67.

Gréve de la Faim Poursuivie depius 8 Ans par un Revendicateur pur. (Hunger strike carried on for 8 years.) Mlle. S. Rousset, G. Daumezon, and J. Masson. 76.

Apparition Tardive de Troubles Psycho-Sensoriels et d'un Syndrome Parkinsonien chez une Kleptomane Vingt Fois Condamnée. (The delayed appearance of psycho-sensorial disturbances with a Parkinsonian syndrome in a kleptomanic convicted 20 times.) P. Scherrer. 88.

Dépersonnalisation, Déréalisation, Aproprioceptivité. Esquisse Anatomoclinique. (Depersonalization, etc. An anatomoclinical sketch.) M. Didé. 95.

Quelques Traitements de Malades du Type Démence Précoce par l'Insuline et le Cardiazol. (Treatment of dementia præcox patients with insulin and cardiazol.) Leulier, Leclercq, and Casalis. 103.

L'Épreuve de Lombard Appliqueé en Psychiatrie. (Contribution a l'Étude des Reflexes Conditionnels.) (The Lombard Test and its application to psychiatry. A contribution to the study of conditioned reflexes.) P. Rubenovitch and J. Pestier. 116.

Syphilis in Certain Psychopathic Syndromes.—Amongst psychopathic states such as those attributed to arteriopathic dementia, progressive dementia præcox, and senile dementia a number of conditions are thought by the author to be really attributable to masked syphilis. He does not attach much value to the negative Wassermann reaction in the C.S.F. in such cases, but considers that the colloidal benzoin curves, the Meinicke and the Takata Ara reactions may when positive demonstrate the existence of an infection of the central nervous system in these cases, though it may be necessary to cause a reactive state in order to demonstrate them. It would not appear that the author has attempted a valuation of these serological reactions which would justify his statements as to the prevalence of larval syphilis in the psychopathic states.

Glossolalia.—This is the fifth case to be described of this rare psychiatric syndrome. The present case is that of a woman of 55 suffering from a paranoid psychosis characterized by multiple hallucinations, mystic ideas, delusions of persecution of a vague unsystematized nature. The intellectual capacity, though never very strong, has not been enfeebled. The language spoken by the patient is not unlike Creole French. It resembles an attempt to deform the French language by supression and literal modifications, whilst conjunctions and prepositions are omitted. It differs from such a patois as the Creole by its poverty in forms of expression. As in all cases of glossolalia the language has a definite fixity as regards the neologisms employed and their sense. The patient has been developing this language, which she claims to be of an inspired origin, for the past ten years.

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Insulin Shock Treatment of Schizophrenic Patients. S. Katzenelbogen, H. E. Harms, and D. A. Clark. 1.

*Vesical Activity in Schizophrenic States Associated with Catalepsy. E. S. Tauber, L. G. Lewis, and O. R. Langworthy. 14.

*Velocity of Blood Flow in Schizophrenia. J. E. Finesinger, M. E. Cohen, and K. J. Thomson. 24.

*Studies in Diseases of Muscle. II. Effect of Varying Amounts of Ingested Creatine on Creatine Tolerance in Progressive Muscular Dystrophy. A. T. Milhorat and H. G. Wolff. 37.

*Enostoses of the Calvarium: Incidence at Autopsies in State Hospitals. M. M. Canavan. 41.

*Nature of the "Silver Cells" Occurring in Multiple

Sclerosis and Other Diseases. N. Blackman and T. J. Putnam. 54.
Clinical Evaluation of Use of Fluids in Treatment of Delirium Tremens. P. Piker. 62.
*Intellectual Deterioration in the Psychoses. W. Malamud and E. M. Palmer. 68.
Malignant Tumor Within the Third Ventricle : Three Cases of Unusual Type with Invasion of the Ventricular Walls. F. R. Ford and W. Muncie. 82.
Electro-Encephalography. III. Normal Differentiation of Occipital and Precentral Regions in Man. H. H. Jasper and H. L. Andrews. 96.
*Friedreich's Ataxia : A Histopathological Study. G. B. Hassin. 116.
*Minerals in Normal and in Pathological Brain Tissue, Studied by Micro-Incineration and Spectroscopy. L. Alexander and A. Meyerson. 131.

Vesical Activity associated with Catalepsy.—Cystometric readings were made on nine patients with catatonic schizophrenia associated with catalepsy. The resting intravesical pressure was usually high during filling of the bladder. Abnormal waves of contraction of the muscle were observed. The bladder in these cases had a greater capacity than normal. Although waves of contraction carried the pressure to 60 cm. of water, no fluid escaped from the urethra. The patients showed no ability to produce voluntary contraction of the muscle at the end of filling. The records showed distinct deviations from the normal. The changes in the vesical activity paralleled the degree of catalepsy. (R. M. S.)

Velocity of Blood Flow in Schizophrenia.—The authors' observations on the rate of blood flow in patients with schizophrenia do not corroborate the conclusion of Freeman that schizophrenia is characterized by an abnormal slowing of the circulation time. (R. M. S.)

Diseases of Muscle.—Feeding experiments on patients with progressive muscular dystrophy led to the following conclusions : When creatine is ingested, the absolute amount retained is not fixed, but is relative and dependent on the amount, within fairly wide limits, of creatine administered. The percentage retention, however, is constant. Only when very large amounts are ingested is the amount retained no longer proportional to the amount administered. In these instances, the absolute amounts retained are constant and apparently represent the maximum capacity of the body to hold exogenous creatine. (R. M. S.)

Enostoses of Calvarium.—A review of 3,250 protocols from hospitals for mental disease shows calvarial enostoses in 230 patients, or 7 per cent. Of these 230 patients, 181 were women and 49 men. The weight of the liver was lowered in 105 cases, the average being 815 gm. One hundred patients were under 5 feet and 6 inches (167·5 cm.) in stature. Seventeen patients were obese, but 53 were emaciated, while the majority were in the " fairly " or the " poorly " nourished group. Seventy-four patients had atrophy of the frontal portion of the brain (a common change in mental disease, but not in mental defect), while 156 did not. In 20 cases in which the pituitary was examined histologically, no constant change was observed. (R. M. S.)

" Silver Cells " in Multiple Sclerosis.—" Silver cells " are characteristic of multiple sclerosis. They appear to be phagocytes of glial origin, as Steiner described, and often contain yellow pigment. They are not confined to multiple sclerosis and syphilis, however. They may occur also in vascular lesions under conditions which appear substantially to exclude the possibility of local phagocytosis of micro-organisms. They have not been observed by previous investigators in cases of a great variety of other conditions used as controls. Small though this material is, it appears sufficient to justify the conclusion that the argentophilic particles are not necessarily of spirochetal or bacterial origin. Their occurrence in vascular lesions, the fact that similar cells contain yellow pigment, and the demonstration in them of what is presumably iron by means of micro-incineration suggest that the silver-staining material may be of hæmatogenous origin. (R. M. S.)

Intellectual Deterioration in the Psychoses.—The present study is an analysis of the performance on the short form of the Stanford-Binet scale of a series of 200 deteriorated psychotic patients and 100 subnormal subjects, in the attempt to find significant differences which may be described in terms of objectively recognizable patterns of scatter differentiating deterioration from congenital defect and giving some insight into its functional nature. The findings may be summarized as follows : The performance of deteriorated psychotic patients differs both quantitatively and qualitatively from that of subnormal subjects at the same mental age level. Not only do psychotic patients tend to scatter more than subnormal persons, but some tests are found to be significantly easier for psychotic than for subnormal subjects and others more difficult. These differences can be described in terms of objectively recognizable patterns of scatter. Such patterns are useful, first, as supplementary diagnostic aids in differentiating deterioration and congenital defect and, second, as means of gaining some insight into the qualitative nature of deterioration. The patterns show a low but definitely positive relationship to the degree of deterioration. No significant relation is found between the patterns and the duration of the disease or the differential diagnosis. On the basis of analysis of the patterns, the hypothesis is advanced that deterioration manifests itself in the material studied in activities requiring the directional control of thought. The study shows the value of psychometry, as furnishing not measurements expressed as a single number or quantity without

meaningful relationship to the phenomena being examined but indexes to both quantitative and qualitative changes in underlying psychic function. (R. M. S.)

Friedreich's Ataxia.—Hassin concludes that the differences in the cord changes in Friedreich's ataxia and subacute combined degeneration are quantitative and are due to the time element; one is chronic degeneration and the other subacute. The medulla, pons, and cerebellum are not involved in Friedreich's disease, but are affected in Marie's ataxia. Lesions observable in the spinal cord in Friedreich's disease often occur in Marie's form, but the olivopontocerebellar changes so typical of the latter do not occur in the former. Friedreich's and Marie's ataxia are different morbid conditions; the one is a disease of certain tracts of nerve fibres, and the other of certain groups of ganglion cells. The degeneration of the posterior roots which often occurs in cases of Friedreich's disease of long standing is secondary to that of the posterior columns, in which it is primary. (R. M. S.)

Minerals in Brain Tissue.—Pathological tissue previously studied in micro-incineration work was subjected to spectroscopic analysis with the following results. The normal cerebral grey matter of the human adult is richer than the white matter in iron, calcium, magnesium, and sodium, while normal white matter is richer in phosphorus. The brain of the new-born human infant is richer in most elements, but poorer in iron, than that of the adult. The lowered iron content seems to correspond to the lesser vascular density of the brain of the newborn. In foci of ischemic necrosis, softening, and multiple sclerosis the alteration in the spectroscopic picture is surprisingly insignificant as compared with the intensive demineralization of the tissue demonstrated by micro-incinerated preparations in these conditions. However, while the tissue itself appears demineralized in micro-incinerated preparations, ample mineral is demonstrated in hypermineralized scavenger and glia cells, which stand out against the otherwise demineralized background of these lesions. Spectroscopic studies justify the conclusion that these scavenger and glia cells contain most of the minerals in about the proportions which normally are distributed evenly within the tissue, except for potassium, which is diminished in freshly softened areas, and for iron, which is increased in all these lesions. The iron in these lesions is probably hæmatogenous and points to vascular dilatation, stasis, or thrombosis in the areas involved. In dementia paralytica there is no absolute increase of iron. This tends to indicate that the loss of iron by decrease of the volume of the vascular bed due to narrowing and obliteration of cerebral blood vessels, especially capillaries, in this disease is greater than the increase of iron by perivascular and intraglial tissue deposits. In lead encephalitis, more lead is deposited in the grey than in the white matter of the brain. In œdematous brain tissue, sodium and calcium are increased. This increase is relatively greater in the white than in the grey matter. The ash of a meningioma was found to be ten times as rich in calcium as the normal grey matter, while the other elements were diminished. The ash of a spongioblastoma of mixed type, with a great deal of protoplasmic and fibrillary astrosytic differentiation, showed more potassium, but less phosphorus and magnesium, than the normal grey matter. (R. M. S.)

Vol. 39. No. 2. February 1938.

Sakel's Pharmacological Shock Treatment for Schizophrenia: Tentative Directions and System of Recording. J. P. Frostig. 219.
Protamine Zinc Insulin: Its Unsuitability for Hypoglycemic Shock. H. H. Reese and A. V. Veer. 232.
Hypoglycemia: Neurologic and Neuropathologic Studies. F. P. Moersch and J. W. Kernohan. 242.
*Results of Treatment of Athetosis by Section of Extrapyramidal Tracts in the Spinal Cord. T. J. Putnam. 258.
*Oxygen and Carbon Dioxide Contents of Arterial and Venous Blood of Schizophrenic Patients. J. M. Looney and H. Freeman. 276.
*Lipoid Content of the Blood in Deficiency Diseases and During Demyelinization of the Nervous System. E. F. Gildea. 284.
Cerebral Dysrhythmias of Epilepsy: Measures for Their Control. F. A. Gibbs, E. L. Gibbs, and W. G. Lennox. 298.
Neural Correlations of Vision and Their Significance for Localization of Tumors of the Brain: A Preliminary Report. C. A. Elsberg and H. Spotnitz. 315.
*Contribution to Problem of Cutaneous Localization in Man. E. Gellhorn, J. Mehlman, and M. Kaplan. 327.
Prepsychotic Personality of Patients with Agitated Depression. W. B. Titley. 333.
Familial Neurosyphilis of the Dementia Paralytica Type. W. C. Menninger and M. Grotjahn. 343.
*Studies in Diseases of Muscle. III. Metabolism of Creatine and Creatinine in Myasthenia Gravis, including a Study of the Excretion of Nucleosides and Nucleotides. A. T. Milhorat and H. G. Wolff. 354.

Treatment of Athetosis by Section of Extrapyramidal Tracts.—A series of 23 patients suffering from involuntary muscular movements of an athetoid character were subjected to section of the anterior column of the spinal cord, the operation being designed to sever the extrapyramidal motor fibres. There were three deaths in the series; 17 of the survivors have shown ranging degrees of improvement for periods up to five years. In the four cases in which there was no improvement, Parkinsonian tremor was present. (R. M. S.)

Blood of Schizophrenic Patients.—The distribution of carbon dioxide in schizophrenic patients is essentially lower than

in normal subjects. So far as the supply of oxygen is concerned, they do not differ from normal subjects, but show a certain degree of dysfunction in its utilization. (R. M. S.)

Blood in Deficiency Diseases.—The lipoids of the blood serum of 12 patients presenting severe symptoms of deficiency disease were studied. No evidence was obtained to indicate that prolonged subsistence on diets sufficiently lacking in vitamins B_1, B_2 (G), and possibly A to produce changes in the nervous system has an effect on the lipoid content of the blood except that due to malnutrition. (R. M. S.)

Cutaneous Localization in Man.—Tactile stimulation of cutaneous sense organs involving pain and warmth endings, respectively, leads to a lesser error in localization than does nontactile stimulation of the same sense organs. This seems to be due to the fact that the touch sense is involved in the tactile experiments, although no conscious touch sensation is elicited. The significance of this phenomenon is discussed. (R. M. S.)

Diseases of Muscle.—The authors suggest that the fundamental metabolic disturbances in myasthenia gravis are not centred in the metabolism of creatinine and creatine, but that the metabolism of creatine is involved secondarily when the abnormal process has become severe. Furthermore, once these metabolic processes are seriously involved, the prognosis for life is grave. (R. M. S.)

Vol. 39. No. 3. March 1938.

*Relation of the Cerebral Cortex to the Grasp Reflex and to Postural and Righting Reflexes. I. Bieber and J. F. Fulton. 433.
*Effect of Experimental Temporary Vascular Occlusion on the Spinal Cord. II. Changes in Mineral Salt Content of Nerve Cells. L. L. Tureen. 455.
*Histopathologic Changes in the Brain in Experimental Hyperinsulinism. A. Weil, E. Liebert, and G. Heilbrunn. 467.
*Organization of Memory Traces in the Korsakoff Syndrome. L. Bender, F. J. Curran, and P. Schilder. 482.
*Variability of Circulation Time in Normal and in Schizophrenic Subjects. H. Freeman. 488.
Spongioblastoma Polare : A Clinicopathologic Study of Twelve Cases. D. H. Echols. 494.
*Psychologic Structure of Catatonia : A Psychopharmacologic Survey of Utilizing Sodium Amytal. M. W. Thorner. 513.
References to Sex Organs and Functions in Speech Productions of Two Preschool Children. A. A. Low. 519.
*Gerstmann Syndrome : Finger Agnosia, Agraphia, Confusion of Right and Left and Acalculia. Comparison of this Syndrome with Disturbance of Body Scheme Resulting from Lesions of the Right Side of the Brain. J. M. Nielsen. 536.

Gerstmann Syndrome.—The Gerstmann syndrome is characterized by finger agnosia, agraphia, confusion of right and left, and acalculia. Nielsen reviews the literature to which he contributes five personally observed cases. (R. M. S.)

Relation of Cerebral Cortex to Grasp Reflex.—Animal experiments led the authors to the following conclusions concerning the mechanism of the grasp reflex : The grasp reflex varies with the position of the body in space, directly with the righting reflexes. The grasp reflex is also to some extent influenced by the neck and labyrinthine reflexes when these are present. The skin receptors are unessential for elicitation of the grasp reflex and evidently play little part in its ordinary production. Stretch of the digital tendons is the most effective stimulus for the grasp ; after complete deafferentation of the arm muscles, tension on the shoulder muscles serves to evoke the grasp in an animal exhibiting the thalamic reflex pattern. When the shoulder muscles have, in addition, been deafferented, the grasp can be elicited by moving the animal rapidly through space. Since the grasp varies, as do the other righting reflexes, with the position of the body and since, if the animal succeeds in grasping an object when in the lateral position, the body is drawn automatically into the horizontal posture, it is concluded that the grasp is an integral part of the body righting reflex mechanism. (R. M. S.)

Experimental Temporary Vascular Occlusion.—The ash residue of anterior horn cells is altered after the spinal cords of rats are subjected to periods of total vascular occlusion. Periods of nonfatal ischemia result in excessive increase in minerals within the nerve cell, which persists in a disorganized manner for about one week. Reorganization of the mineral structure commences in one week and is not complete until after one month. Periods of fatal ischemia result in loss of minerals, which continues until the intracellular and the extracellular salts are equal. Functional activity is regained after sublethal injury at a time when excessive mineralization has begun, and the increase in minerals continues for several days longer. Vascular endothelial and neuroglia cells exhibit hypermineralization at a time when they are most actively proliferating. (R. M. S.)

Histopathologic Changes in Brain in Hyperinsulinism.—The pathologic changes induced by hyperinsulinism appear to be the result of anoxæmia—not anoxæmia from lack of oxygen following vascular disturbance, but intracellular anoxæmia, i.e. the inability to utilize oxygen in the presence of large doses of insulin. (R. M. S.)

Memory Traces in Korsakoff Syndrome.—The authors conclude that the psychology of the Korsakoff syndrome cannot be understood merely from the point of view of the

fading of memory traces. There is a different type of organization comparable with organizations in childhood and, under special conditions, in the normal person. (R. M. S.)

Circulation Time in Normal and Schizophrenic Subjects.—On the average, schizophrenic patients have an abnormally slow and a highly variable rate of blood flow. (R. M. S.)

Psychologic Structure of Catatonia.—Four common, definite, and related symptom groups found in catatonic patients were investigated by a psychopharmacological method. In these patients, who are otherwise approached with difficulty, a supporting structure was sought for the symptoms presented. Inability to choose among different lines of action was the only constant, fundamental factor found and is considered the most constant psychological basis on which the catatonic reaction rests. The other phenomena noted did not occur with sufficient frequency to be considered as other than conditioning factors which, with the psychosomatic peculiarities of a given patient, determine the variations noted clinically within the diagnostic limits of the catatonic group. (R. M. S.)

ARCHIV FÜR PSYCHIATRIE UND NERVENKRANKHEITEN

Vol. 108. Nos. 1 and 2. April 1938.

*Die "systematischen Atrophien." Eine wohlgekennzeichnete Gruppe der Erbkrankheiten des Nervensystems. ("Systematized atrophies." A well-defined group of hereditary nervous diseases.) H. Spatz. 1.

Endemische und epidemische Thyreopathie in ihrer Abhängigkeit von Boden und Klima. Ein epidemiologischer Beitrag zum Kropfproblem. (Endemic and epidemic thyreopathy. An epidemeological contribution to the problem of goitre.) F. Wolter. 19.

Beiträge zur funktionellen Gliederung des Corpus geniculatum laterale des Menschen. (The functional subdivision of the external geniculate body in man.) A. Juba. 85.

*Statistisches zur Frage der akuten und chronischen Encephalitis epidemica. (Statistical investigation on acute and chronic epidemic encephalitis.) H. Nagel. 94.

Eine rasche Bindegewebsimpregnationsmethode des Zentralnervensystems, besonders für Geschwülste. (Rapid impregnation method for the mesodermal tissue in the central nervous system, particularly for tumours.) A. Bonkáló. 102.

Zur Frage der chronischen Poliomyelitis. (On chronic poliomyelitis.) H. Lange. 105.

Chemie und psychiatrische Shocktherapie. (Chemistry and psychiatric shock treatment.) J. Schuster. 120.

*Ueber eine systematische Atrophie der Oberen Olive. (Atrophy of the superior olive.) E. Weisschedel. 219.

Formen des Aberglaubens im Schwarzwald. (Superstition in the Black Forest.) K. Beringer. 228.

Ueber 2 Fälle von Trigeminustumoren mit Zwischenhirnsymptomen. (On two cases of trigeminal tumours with diencephalic symptoms.) W. Birkmeyer and J. Silberpfennig. 255.

Systematized Atrophies of Central Nervous System.—An attempt is made to delineate atrophic processes from degeneration, necrobiosis, and so forth. Atrophies of system character include conditions such as Pick's disease, olivo-ponto-cerebellar atrophy (now called atrophy of the pes pontis and inferior olive), posterior tract degenerations, atrophy of the peripheral motor neurone, and so forth. Many of these conditions are hereditary diseases, but it would be a mistake to postulate an anatomical criterion for heredity. The paper is rich in detail which must be read in the original. (A. M.)

Statistics of Epidemic Encephalitis.—Details of 362 encephalitics who were treated in one hospital in Munich are summarized. The largest number of acute cases occurred during the period 1918–1920 and the months of January, February, and March show the highest incidence. The frequency with which various symptoms occurred are given. The more interesting findings regarding the chronic stage are as follows: Sluggish reaction to light with good reaction to accommodation was found in 17·7 per cent., nystagmus in 20·4 per cent., facial palsy in 30·6 per cent., sensory disturbances in 5·4 per cent., compulsion symptoms in 8·3 per cent., and epileptiform seizures in 2·8 per cent. When the interval between acute and chronic stage was investigated it was shown that 36·5 per cent. of the patients had some signs of Parkinsonism immediately following the acute stage. (S. L. L.)

Atrophy of the Superior Olive.—In eight cases of Huntington's chorea, one case of Friedreich's ataxia, and one case of atrophy of the cerebellar cortex a primary symmetrical atrophy confined to the superior olive was found. The involvement of this centre does not interfere with the function of hearing. (A. M.)

Vol. 108. No. 3. June 1938.

*Ueber den quantitativen mikrochemischen Nachweis von Alkohol im Liquor cerebrospinalis. (Quantitative microchemical method for alcohol in the cerebrospinal fluid.) E. Gabriel and S. Novotny. 279.

Pathographie des französischen Symbolisten Paul Verlaine. (Pathography of the French symbolist Paul Verlaine.) V. Luniatschek. 301.

Ueber die Wirkung von Spiraea ulmaria und Alisma plantago auf das Zentralnervensystem. (The

effect of spiræa ulmaria and alisma plantago upon the central nervous system.) R. Adelheim, C. Amsler, E. Rentz, V. Nicolajev. 338.
*Leberschädigung durch Impf malaria. (Damage to the liver following malaria treatment.) J. Jung and A. Kratky. 346.
Zur Frage der Schädigung des Zentralnervensystems durch Kurzwellenbehandlung. (Damage to the central nervous system following treatment by ultra-short waves.) O. Schiersmann. 363.
*Fehldiagnosen bei Stirnhirntumoren. (Fallacies in the diagnosis of tumours of the frontal lobe.) R. Lemke. 381.
Der Markgehalt von Hirnzentren bei der makroskopischen Färbemethode von Mulligan. (The myelin content of brain centres demonstrated by the macroscopic method of Mulligan.) H. Scheibe. 391.
*Ueber das Elektrenkephalogramm des Menschen. (The electroencephalogram in man.) H. Berger. 407.
Hydrocephalus internus mit hypophysären Erscheinungen. (Internal hydrocephalus with hypophyseal symptoms.) Takeya-Siko. 432.
Zur Kritik der Reflex-Epilepsie. (Critical study of reflex-epilepsy.) A. Feitig. 439.
Das Schweizerische Strafgesetzbuch (21. Dez. 1937) verglichen mit der Strafrechtsreform in Deutschland vom psychiatrischen Standpunkt. (The Swiss penal code (21st December, 1937) compared with the German penal reform from the psychiatric viewpoint.) E. Schultze. 469.

Microchemical Method for Determination of Alcohol.—By means of Widmark's micromethod it was found that under normal circumstances the alcohol content was five times greater in the blood than in the cerebrospinal fluid. There was no significant difference in various psychoses except in delirium tremens. After intake of ¼ litre of a 15 per cent. solution of alcohol the amount in the cerebrospinal fluid reached higher values than that in the blood and decreased more slowly to the norm. Even after 6½ hours there was still an increase in the cerebrospinal fluid, at a time when the blood values were again normal. The authors point out the practical significance of their findings. (A. M.)

Damage to Liver Following Malaria Treatment.—The authors studied the damage done to the liver of paretics who had been treated with malaria. Recent as well as late cases show marked parenchymatous changes. A reduction of the mortality has been brought about by giving glucose injections and avoiding the intravenous route for the inoculation. (S. L. L.)

Diagnosis of Tumours of Frontal Lobe.—Details of three cases are given. In two of them the diagnosis was only made when calcified tumours were shown by X-ray. In the third case a diagnosis of schizophrenia was made and treatment with insulin was started. The patient died during treatment and a large glioma was found. The author stresses the fact that frontal tumours can produce psychoses which are very unlike the usual exogenous reaction type. (S. L. L.)

The Electro-encephalogram in Man.—In the first part of this paper Berger deals with the findings in epilepsy. He reports his failure to obtain electrencephalograms (E.G.G.) during a complete fit. The fit, however, is followed by a period during which the alpha-waves have disappeared while the beta-waves have increased. This is followed by slow alpha-waves which according to the author are identical with the delta-waves of others. During petit-mal the alpha-waves are often replaced by high beta-waves also, or they combine to form slow waves. In the second part more general problems are discussed and the author repeats his statement that the alpha-waves do not originate in the occipital lobe or any other areas, but in the lower layers of the whole cortex, whereas the beta-waves come from the upper three layers. (S. L. L.)

BRAIN

Vol. 61. No. 2. June 1938.

*Some Observations on Headache. D. W. C. Northfield. 133.
*" Aphasia " in a Partial Deaf-Mute. M. Critchley. 163.
*Gliomatosis Cerebri. S. Nevin. 170.
*Subacute Diffuse Ependymitis. R. M. Stewart. 192.
*The Central Pathway in Man of the Vasomotor Response to Pain. D. G. Marquis and D. J. Williams. 203.
*Vasomotor Control of Cerebral Vessels. H. S. Forbes and S. S. Cobb. 221.

Observations on Headache.—An analysis of 100 consecutive cases of brain tumour showed that headache was the initial symptom in 83 per cent. of posterior fossa tumours and in 30–40 per cent. of supratentorial tumours. Headache was never the initial symptom in 9 cases of acoustic neurinoma. In 42 cases with unilateral headache the tumour was situated on the same side in 32 cases and in 6 cases was in the mid-line. Pain in the neck was present in 22 per cent. of supratentorial tumours and in 49 per cent. of infratentorial. In most cases frontal headache was also present. Headaches could not be related to the absolute level of the C.S.F. pressure, but was associated with sudden changes in pressure. This was thought to be due to the disturbance of the intra- and extra-vascular pressure relationship. The sensation was thought to arise from the cerebral rather than from the dura vessels, because tying the middle meningeal artery did not influence histamine headache. Histamine injected into the internal carotid artery produced headache, but not when injected into the external carotid. The afferent pathway for the sensation of headache appeared to vary because unilateral section of the 5th nerve was successful in abolishing histamine headache on that side in only three out of five cases. (J. D.)

" Aphasia " in a Partial Deaf-Mute.—A

left-sided vascular lesion developed in a man of 42 who had been deaf since the age of 7. He was subsequently unable to write and had a marked defect in the ability to make signs, and what little vocal speech had remained was also disturbed. Associated with the aphasia was a slight right-sided facial weakness and hemihypæsthesia. The cause of the aphasia appeared to be not apraxia but a disturbance in the preverbal processes. (J. D.)

Gliomatosis Cerebri.—A full report of three cases of diffuse neoplastic overgrowth of cerebral glial cells is presented, together with a review of the literature. The condition is probably a primary blastomatous malformation arising upon a congenital developmental defect. (J. D.)

Subacute Diffuse Ependymitis.—A case of subacute diffuse ependymitis is reported. The ependyma of the ventricular system was the site of a marked subacute inflammatory process which had caused partial occlusion of the iter with subsequent internal hydrocephalus. (J. D.)

Vasomotor Response to Pain.—The vasoconstriction of the digital vessels in response to a painful stimulus has been investigated in patients with lesions of the sensory pathways. In each subject the average response to stimuli applied to an area of normal sensibility was compared with that from stimulation of areas of disturbed sensibility. In lesions below the thalamus the vasomotor response was affected in the same way as sensation, while in lesions of the thalamus or cortex the vasomotor responses from stimulation of normal and affected areas were equal. It was concluded that in man the ascending pathway for the vasomotor response to somatic stimulation is the spinothalamic tract, and that the vasomotor reflex arc is complete in the brain stem below the level of the sensory thalamus. (J. D.)

Vasomotor Control of Cerebral Vessels.—A review of the recent work together with some observations on the control of the cerebral blood vessels is reported. It is concluded that vasoconstrictor and probably also vasodilator nerves exist, but that their influence is comparatively slight and their function likely only to prevent undesirable fluctuations in vessel calibre and to assist in diverting blood from one area to another. (J. D.)

BULLETIN OF THE NEUROLOGICAL INSTITUTE OF NEW YORK

Vol. 7. No. 1. March 1938.

*The Hippocampus and Its Relation to the Corpus Callosum. F. Tilney. 1.
*The Relative Refractory Period of Olfaction and of Vision. H. Spotnitz and C. A. Elsberg. 78.

Hippocampus and Corpus Callosum.—In this first section of a paper on the hippocampus and corpus callosum the development of these structures, both from the embryological and comparative points of view has been comprehensively described. The unitary structural nature of the archipallium has been stressed along with the variations in it due to the development of the corpus callosum and lateral ventricles. (J. D.)

Refractory Period of Olfaction and Vision.—The relative refractory period of visual processes is described and attributed to a central mechanism. This is correlated to the refractory period of other nervous processes. (J. D.)

CLINICAL SCIENCE

Vol. 3. No. 2. April 1938.

Insulin Resistance and the Arterio-Venous Blood-Sugar Difference. W. J. Griffiths. 91.
The Effect of Different Diets on the Insulin Sensitivity of Diabetes. W. I. Card. 105.
The Blood Circulation in the Human Limb : Observations on the Differences between the Proximal and Distal Parts and Remarks on the Regulation of Body Temperature. R. T. Grant and R. S. Bruce Pearson. 119.
Effects of Asphyxia and Pressure on Sensory Nerves of Man. T. Lewis and E. E. Pochin. 141.
Observations on the Blood Circulation in Voluntary Muscle in Man. R. T. Grant. 157.
*Observations on Referred Pain Arising from Muscle. J. H. Kellgren. 175.
*Delay of Pain Perception in Tabes Dorsalis. E. E. Pochin. 191.
*Unilateral Retraction of the Upper Lid in Graves' Disease. E. E. Pochin. 197.
Some Observations on Renin, a Pressor Substance contained in Normal Kidney, together with a Method for Its Biological Assay. G. W. Pickering and M. Prinzmetal. 211.
*Further Observations on Familial Periodic Paralysis. E. N. Allott and B. McArdle. 229.
The Effect of Adrenalin on the Serum Potassium Level in Man. L. I. M. Castleden. 241.

Referred Pain arising from Muscle.—Pain from deep structures was induced by the injection of hypertonic saline. Fascia and tendons give localized pain, while muscles give diffuse pain which is referred. The area of reference is associated with tenderness which is abolished by the injection of novocaine into the area while the pain is not affected. The distribution

of the pain follows a segmental pattern which differs from that of the segmental innervation of the skin. (J. D.)

Delay of Pain Perception in Tabes.—The length of the delay of pain perception in tabetics has been measured and the time found to correspond to that necessary for the appreciation of second pain in normal subjects. It was concluded that the delay in tabes was not due to an abnormal slowing of the impulses, but to a defect in those pain fibres which conduct rapidly. (J. D.)

Unilateral Retraction of Upper Lid in Graves' Disease.—Upper lid retraction and exophthalmos have been found to occur independently in cases of Graves' disease. The characteristics of each have been examined in unilateral cases. Lid retraction is manifested by the upper lid being separated from the pupil by a greater gap than normal, by elevation of the lower lid, and by a wrinkle of skin across the upper lid. Exophthalmos is characterized by protrusion of the eyeball and exposure of the sclera between the cornea and lower lid. (J. D.)

Familial Periodic Paralysis.—In two further cases a fall in serum potassium has been found to be associated with an attack of familial periodic paralysis and relief was obtained by the administration of potassium. During attacks potassium was retained in the body. The level of serum potassium at which paralysis became evident in different cases varied and lower values have been found in ketosis without paralysis. Changes in phosphorus metabolism paralleled those in potassium and it appeared that the mechanism of the attacks was related to an abnormality involving hexosephosphate. (J. D.)

JOURNAL BELGE DE NEUROLOGIE ET DE PSYCHIATRIE

Vol. 38. No. 4. April 1938.

Quelques Réflexions sur le Syndrome de Guillain-Barré. (Some reflections on the syndrome of Guillain-Barré.) H. Roger and J. Boudouresques. 243.

Radiculonévrite avec Dissociation Albumino-Cytologique du Liquide Céphalo-Rachidien (Syndrome de Guillain et Barré) chez l'Enfant. (Radicular neuritis with dissociation between albuminuria and cells in the C.S.F. in an infant.) P. Giraud and J. Boudouresques. 256.

Les Polyradiculonévrites Aiguës (Syndrome Guillain-Barré-Strohl). (The acute polyradiculitides.) Riser and Planques. 264.

Les Polyradiculonévrites Crâniennes Bilatérales avec Dissociation Albumino-Cytologique. (Bilateral cranial polyneuritis with dissociation between albuminuria and cells in the C.S.F.) L. v. Bogaert and M. Maere. 275.

Remarques sur quelques Observations de Polyradiculonévrites avec Dissociation Albumino-Cytologique et à évolution Favorable (Contribution à l'Étude des Maladies du Neurone Périphérique.) (Remarks on some observations in polyneuritis.) J. Dagnelie. 282.

A Propos de Trois Enfants Présantant Certains Caractères du Syndrome de Guillain-Barré. (Notes on three children presenting certain signs of the syndrome of Guillain-Barré.) Cohen. 306.

Considérations Diverses sur le Syndrome de Polyradiculonévrite avec Dissociation Albumino-Cytologique. (Diverse remarks on the syndrome of polyneuroradiculitis.) J. A. Barré. 313.

Synthèse de la Discussion. (Conclusions of the discussion.) G. Guillain. 322.

The above papers are a series dealing with one clinical syndrome. Many points of interest are raised by the different authors. (E. A. C.)

Vol. 38. No. 5. May 1938.

Les Réactions Hystéro-Mentales et le Problème de leur Réalité Biologique. (The problem of the biological existence of mental hysterical states.) R. Nyssen. 331.

La Thérapeutique des Anomalies Sexuelles Graves par la Castration. (The treatment of sexual disorders by castration.) J. Ley. 344.

Des Variations de la Glycémie Provoquées par l'Injection de Pentaméthylène-tétrazol chez les Schizophrènes. (The alteration in blood sugar produced by the injection of penta-methylene-tetrazol in schizophrenics.) P. Clémens. 357.

De l'Inspection des Services Ouverts par les Pouvoirs Publics. (The inspection of psychiatric institutions by public authorities.) J. Titeca. 366.

Le Traitement Convulsivant par le Penta-méthylène-tétrazol calme l'Agitation Périodique de Certains Épileptiques. (The convulsant treatment with penta-methylene-tetrazol calms the periodic agitation of some epileptics.) A. Leroy. 377.

Vol. 38. No. 6. June 1938.

*Une Nouvelle Méthode d'Imprégnation des Neurofibrilles. (A new neuro-fibrillar impregnation method.) A. Dewulf. 407.

Le Problème de la Localisation et des Ataxies Corticales. (The problem of localization in the cerebral ataxias.) M. A. Gerebtzoff. 411.

Hémi-Hypertrophie Alterne Cranio-Acrale avec Imbécillité. (Hemi-hypertrophy of the skull with imbecility.) F. Verschueren. 431.

*Étude Électrencéphalographique de Deux Cas d'Anesthésie Hystérique. (Electro-encephalographic studies in two cases of hysterical anæsthesia.) J. Titeca. 442.

Ramoelissement Cérébral et Troubles Mentaux. (Cerebral softening and mental symptoms.) M. Leroy. 479.

Neuro-fibrillar Impregnation Method.—By this method it is possible to stain formol-bromide fixed tissue for neuro-fibrils. (E. A. C.)

Electro-encephalographic Studies of Hysterical Anæsthesia.—On applying a sensory stimulus to the normal half of the body, the Berger rhythm was interrupted; stimulation of the anæsthetic region caused no similar change in Berger rhythm. In the second case cerebral action potentials of greater amplitude were obtained than in the normal subject: these were not altered by applying a stimulus to the anæsthetic half of the body. The author discusses these observations. (E. A. C.)

Vol. 38. No. 7. July 1938.

Hématome Intracérébral non traumatique. Opération-Récuperation. (Non-traumatic intracerebral hæmatoma. Operation and recovery.) L. Laruelle and L. Massion-Verniory. 495.
Sur la Pathogénie des Troubles Vestibulaires dans les Lésions de la Moelle Épinière. (On the cause of vestibular troubles in lesions of the spinal cord.) J. Helsmoortel. 504.
Les Chances de Survie et de Guérison des Paralytiques Généraux. (The chances of survival and cure in general paralysis.) P. Vervaeck. 508.
Anomalie Vertébrale et Troubles Radiculaires. (Vertebral anomaly and Root Affections.) M. Leroy. 520.
De la Valeur de l'Épreuve au Cardiazol en Tant que Test Diagnostique de l'Épilepsie. (The value of cardiazol as a test in epilepsy.) G. Muyle. 525.
Le Cahier des Revendications à Présenter par les Psychiatres à l'Autorité Judiciaire. (Certificates presented by psychiatrists to judicial authorities.) R. Titeca. 531.
Influence Stimulante du Produit β Phényl-Isopropylaminsulfate (Actédrone) sur l'Activité Psychique et sur l'Humeur à l'État Physiologique et Pathologique. (The stimulating influence produced by β phenyl-isopropylaminsulphate on psychiatric activity and in the temperament in physiological and pathological states.) T. de Lehozky. 537.

JOURNAL OF CLINICAL INVESTIGATION

Vol. 17. No. 3. May 1938.

The Effect of Eclamptic Blood upon the Urinary Output and Blood Pressure of Human Recipients. E. W. Page. 207.
Studies in the Physiology of Artificial Fever. 1. Changes in the Blood Volume and Water Balance. J. G. Gibson and I. Kopp. 219.
Effect of Insulin on the Concentration of Uric Acid in the Blood. E. F. Rosenberg. 233.
Studies of the Circulation in Patients Suffering from Spontaneous Myxedema. H. J. Stewart, J. E. Deitrick, and N. F. Crane. 237.
Heat Stroke. Clinical and Chemical Observations on 44 Cases. E. B. Ferris, M. A. Blankenhorn, H. W. Robinson, and G. E. Cullen. 249.
The Measurement of the Tubular Excretory Mass, Effective Blood Flow, and Filtration Rate in the Normal Human Kidney. H. W. Smith, W. Goldring, and H. Chasis. 263.
The Effect of Alcohol on the Water and Electrolyte Balance in Man. W. M. Nicholson and H. M. Taylor. 279.
Estimations of the Work of the Heart During and Between Attacks of Angina Pectoris. I. Starr, C. J. Gamble, J. S. Donal, and L. H. Collins. 287.
Critical Remarks on the Determination of Urinary Excretion of Ascorbic Acid. M. van Eekelen and M. Heinemann. 293.
The Guanidine Bases in the Blood of Dogs with Experimental Hypertension Produced by Constriction of the Renal Arteries. C. G. Child. 301.
The Effect of Vitamin-D on Calcium and Phosphorus Metabolism: Studies on Four Patients. F. Albright and H. W. Sulkowitch. 305.
A Comparison of the Effects of A.T. 10 (Dihydrotachysterol) and Vitamin-D on Calcium and Phosphorus Metabolism in Hypothyroidism. F. Albright, E. Bloomberg, T. Drake, and H. W. Sulkowitch. 317.
Evaporation of Body Water in Lobar Pneumonia. G. K. Anderson. 331.
Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia. VII. Resemblances between the Proteolytic Activity of Normal Human Gastric Juice on Casein in Neutral Solution and the Activity of the Intrinsic Factor. F. H. L. Taylor, W. B. Castle, R. W. Heinle, and M. A. Adams. 335.
The Excretion of Urea in Normal Man and in Subjects with Glomerulonephritis. H. Chasis and H. W. Smith. 347.
The Effect of Total Sympathectomy on the Occurrence of Shock from Hemorrhage. N. E. Freeman, S. A. Shaffer, A. E. Shecter, and H. E. Holling. 359.

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A Simple Method for the Estimation of Total Protein Content of Plasma and Serum.
I. A Falling Drop Method for the Determination of Specific Gravity. 369.
II. The Estimation of Total Protein Content of Human Plasma and Serum by the Use of the Falling Drop Method. B. M. Kagan. 373.
*The Chemical Composition of Voluntary Muscle in Muscle Disease: A Comparison of Progressive Muscular Dystrophy with other Diseases together with a Study of Effects of Glycine and Creatine Therapy. J. G. Reinhild and G. R. Kingsley. 377.
*The Late Effects of Bilateral Carotid Sinus Denervation in Man. R. B. Capps and G. de Takats. 385.
The Renal Factor in Arterial Hypertension with Coarctation of the Aorta. D. A. Rytand. 391.
The Effects on the Cardiovascular System of Fluids Administered Intravenously in Man. II. The Dynamics of the Circulation. M. D. Altschule and D. R. Gilligan. 401.
Changes in Blood and Interstitial Fluid Resulting from Surgical Operation and Ether Anesthesia. J. D. Stewart and G. M. Rourke. 413.
Observations on the Blood of Workmen exposed to High Temperatures. P. L. McLain and E. S. Montgomery. 417.
The Nature of the Lowered Resistance to Infection in Diabetes Mellitus. A. Marble, H. J. White, and A. T. Fernald. 423.
On the Actions of Crystalline Vitamin D_2 (Calciferol) in Chronic Parathyroid Tetany. G. Klatskin. 431.
Cyanosis without Sulf- or Methemoglobinemia in Patients Receiving Sulfanilamide Treatment. L. C. Chesley. 445.
Studies of the Circulation in the Presence of Abnormal Cardiac Rhythms. Observations Relating to (Part I) Rhythms Associated with Rapid Ventricular Rate and to (Part II) Rhythms Associated with Slow Ventricular Rate. H. J. Stewart, J. E. Deitrick, N. F. Crane, and W. P. Thompson. 449.
A Study of Some of the Physiological Effects of Sulfanilamide. I. Changes in the Acid Base

Balance. A. F. Hartmann, A. M. Perley, and H. L. Barnett. 465.
An "Acid" Phosphatase Occurring in the Serum of Patients with Metastasizing Carcinoma of the Prostrate Gland. A. B. Gutman and E. B. Gutman. 473.
Reactions of Human Subjects to the Injection of Purified Type Specific Pneumococcus Polysaccharides. M. Finland and J. W. Brown. 479.
Tissue Pressure (Intracutaneous, Subcutaneous, and Intramuscular) as Related to Venous Pressure, Capillary Filtration, and other Factors. H. S. Wells, J. B. Youmans, and D. G. Miller. 489.
*Proceedings of the Thirtieth Annual Meeting of the American Society for Clinical Investigation Held in Atlantic City, N.J., May, 1938. 501.

Voluntary Muscle in Muscle Disease.—There was a greater variation from the normal in the chemical composition of muscles from cases of progressive muscular dystrophy than in secondary atrophy of the muscle. This was shown in a diminution of creatine and acid extractable substances in progressive muscular dystrophy. (J. N. C.)

Bilateral Carotid Sinus Denervation.—Two cases with bilateral carotid sinus denervation and bilateral cervico-dorsal sympathectomy have been studied. Some months after the operations, no elevation of blood pressure or of pulse rate was observed, but a marked postural hypotension was found. (J. N. C.)

Proceedings of 30th Annual Meeting.

Among a number of papers, the following were of interest :

Familial Periodic Paralysis. (*a*) J. W. Ferrebee, D. W. Atchley, and R. F. Loeb. 504 ; (*b*) R. H. Pudeng, J. F. McIntosh, and D. McEachern. 530.

Chemical studies of the blood were undertaken in single cases and a low potassium content of the blood found during attacks. No other significant chemical abnormalities were found.

Choline Esterase of Muscle in Myasthenia Gravis. W. C. Stadie and M. Jones. 536.

The muscle esterase content in a case of myasthenia was found to be normal. The beneficial effect of prostigmine was not due to an inhibition of muscle esterase. (J. N. C.)

JOURNAL OF COMPARATIVE NEUROLOGY

Vol. 68. No. 3. April 1938.

*Efferent Connections of the Flocculonodular Lobe in the Macaca Mulatta. R. S. Dow. 297.
*The Relations of the Fascia Dentata, Hippocampus and Neocortex and the Nature of the Subiculum. A. A. Abbie. 307.
Study of the Nissl Pattern in the Motor Cells of the Hind Brain of the Lizard (Tackydromus Septentrionalis) under Various Conditions. W. C. Chow. 335.
Studies on the Developing Behaviour of Anura. K. A. Youngstrom. 351.
The Prenatal Growth of the Cat. VII. The Growth of the Brain and of Its Parts, of the Spinal Cord and of the Eyeballs. H. B. Latimer. 381.
The Weights of the Brain and of Its Parts, of the Spinal Cord and of the Eyeballs in the Adult Cat. H. B. Latimer. 395.

Flocculonodular Lobe.—Discrete lesions were made in the flocculonodular lobe of the M. mulatta and the degenerated fibres subsequently traced. It was found that the flocculus sends all its fibres to the nuclei of Deiters and Bechterew. The nodulus and uvula send fibres to the fastigial nucleus, to the dorsal reticular formation, to the vestibular nuclei and to the medial longitudinal bundle. (J. D.)

Hippocampus and Neocortex.—Serial sections of the brains of a group of primitive mammals have been examined. It appeared that the fascia dentata, hippocampus, and adjoining neocortex develop from the same layer of cells, but the arrangement is distorted by the development of the corpus callosum. (J. D.)

Vol. 68. No. 4. June 1938.

*A Nervous Structure in the Pineal Body of the Monkey. P. M. Levin. 405.
*The Exact Origin of the Cortico-Spinal Tract in the Monkey. P. M. Levin and F. K. Bradford. 411.
*The Optically Excitable Cortex in the Rabbit. J. L. O'Leary and G. H. Bishop. 423.
*Further Determinations of the Numbers of Fibres and Cells in the Dorsal Roots and Ganglia of the Cat. D. Duncan and L. L. Keyser. 479.
*Experiments on the Corpus Striatum and Rhinencephalon. D. M. Rioch and C. Brenner. 491.

Nervous Structure in Pineal Body of Monkey.—It has been found that the pineal body of several species of monkey contains a structure composed of fine myelinated fibres and numerous ganglion cells. Its connections are described. (J. D.)

Origin of Cortico-Spinal Tract.—By means of retrogade cell degeneration it has been found that the cortico-spinal tract in the monkey arises mostly from area 4 of Brodmann. However, some 20 per cent. arises from pyramidal cells in the parietal cortex. Area 4 may be divided into a narrow anterior zone which has no pyramidal system and a broad posterior zone which gives rise to the pyramidal projection. (J. D.)

Optically Excitable Cortex.—On electrical stimulation of the optic nerves changes in potential are found in the occipital cortex. The structure of this area of cortex in the rabbit has been studied as has also the spread of electrical activity in it. The possible correlations of the results of the two methods are indicated. (J. D.)

Dorsal Root Fibres and Cell Ratios.—The previous finding of a 1 : 1 ratio between the dorsal root fibres and the cells of the posterior root ganglia has been confirmed in the cat. The percentage of unmyelinated fibres in the posterior roots was found to vary from 2·8 in the first cervical to 77·6 in the eleventh thoracic. (J. D.)

Corpus Striatum and Rhinencephalon.—Destruction and stimulation of the corpus striatum in cats and guinea-pigs which had previously had excision of the ipsilateral motor cortex gave no results attributable to the corpus striatum itself. It was suggested that this system has no autonomous function, but only acts in conjunction with other forebrain systems. The results of stimulation of the brain stem in seven decorticated cats are reported. After removal of the neocortex certain aspects of the normal disposition were retained. (J. D.)

JOURNAL OF MENTAL SCIENCE

Vol. 84. No. 349. March 1938.

*The Impedance Angle and its Relation to Thyroid Treatment in Mental Disorder. W. Sargant, R. Fraser, and M. A. B. Brazier. 255.
Some Observations on the Theory of Perception. S. Sharman. 273.
Imagery and its Relation to Schizophrenic Symptoms. L. H. Cohen. 284.
Disturbances of Consciousness after Head Injuries : Observations on Boxers. E. Guttman and C. E. Winterstein. 347.
Studies in Hay-Fever Patients (the Allergic Personality). E. Wittkower. 352.
Experiments on the Origin of the Wassermann Reaction in the Cerebro-spinal Fluid. A. Beck. 370.
The Takata Reaction on the Cerebro-spinal Fluid in Syphilis of the Nervous System. H. H. Fleischhacker. 378.
The Boarding-out of Mental Patients in the Scottish Highlands. J. A. W. Stone and A. E. Evans. 381.

Impedance Angle.—By means of the impedance angle it was possible to select cases of mental disorder suitable for thyroid therapy and to control the dosage of thyroid. (E. A. C.)

Vol. 84. Nos. 350–351. May–July 1938.

Neurogenesis and the Development of "Synapses," with Particular Reference to the Conditions in Lepidosiren Paradoxa. T. Jones. 451.
Determinants of Physique. J. I. Cohen. 495.
Mental Testing in Male Adolescent Delinquents. F. H. Taylor. 513.
The Treatment of Mental Disorders and Mental Deficiency in Continental Criminal Law. H. Mannheim. 524.
*The Estimation of Vitamin-C Content of the Urine of Fifty Patients Suffering from Psychoses. L. Minski. 541.
Enhancement of Physical and Mental Capacity following Treatment of Chronic Infective Disease. H. F. Fenton. 544.
Head Injuries and Mental Disorder. T. C. Graves. 552.
The Ætiology of the Confusional Syndrome and the Use of T.A.B. Vaccine. D. N. Parfitt. 563.
Six Months' Experience with Cardiazol Therapy. G. S. Nightingale. 574.
Histamine and Insulin in the Treatment of Schizophrenia and Other Mental Diseases. H. Hill. 581.

Vitamin-C Content of Urine.—The average daily output of Vitamin-C in the urine was examined in 50 patients—13 depression, 7 epilepsy, 3 involutional depression, 3 Korsakow's syndrome, and 2 cerebral arterio-sclerosis. The output of these patients was lower than the output of members of the staff on the same diet. (E. A. C.)

JOURNAL OF NEUROPHYSIOLOGY

Vol. 1. No. 3. May 1938.

Limits of Variation of the Synaptic Delay of Motoneurons. R. Lorente de Nó. 187.
Synaptic Stimulation of Motoneurons as a Local Process. R. Lorente de Nó. 195.
Analysis of the Activity of the Chains of Internuncial Neurons. R. Lorente de Nó. 207.
*Localization of Cerebral Lesions by Electroencephalography. J. T. Case and P. C. Bucy. 245.
The Effects of Ablation of the Cortical Motor Face Area in Monkeys. H. D. Green and A. E. Walker. 262.
*Cell-Changes in Some of the Hypothalamic Nuclei in Experimental Fever. L. O. Morgan. 281.

Electro-Encephalography in Cerebral Lesions.—The authors summarize by stating that "intracranial lesions are indicated and may usually be localized by the following electro-encephalographic phenomena : (1) very slow swings, 1 to 2 in five seconds ; (2) slow waves from $\frac{1}{2}$ to 3 per second ; (3) spikes and saw-tooth forms ; (4) electrical manifestations of localized epileptic seizures ; (5) absence of or marked difference in the alpha rhythm on the two sides ; (6) marked diminution or localized absence of electrical activity. Eleven cases are presented, in all of which the lesions have been localized more or less accurately by this method and which collectively show most of the above features." (E. A. C.)

Cell Changes in Fever.—Experimental hyperthermia has been produced in dogs mainly by means of injection of typhoid toxin. A variable amount of chromatolysis was observed in three nuclei of the hypothalamus. (E. A. C.)

Vol. 1. No. 4. July 1938.

Zur Elektrodenanordnung bei den Registrierungen bioelektrischer Potentialschwankungen der Hirnrinde. (The arrangement of electrodes for the registration of action potentials of the cortex.) A. E. Kornmüller and J. A. Schaeder. 287.
The Influence of Hypoglycemia on the Sensitivity of the Central Nervous System to Oxygen Want. E. Gellhorn, R. C. Ingraham, and L. Moldavsky. 301.
The Distribution of the Alpha Rhythm over the Cerebral Cortex of Normal Man. M. A. Rubin. 313.
Effects of Blood Pressure Changes on Cortical Potentials During Anesthesia. H. K. Beecher, F. K. McDonough, and A. Forbes. 324.
Inhibition and Impulse Summation at the Mammalian Neuromuscular Junction. C. A. Maaske, T. E. Boyd, and J. J. Brosnan. 332.
Autonomic Activity and Brain Potentials Associated with "Voluntary" Control of the Pilomotors. D. B. Lindsley and W. H. Sassaman. 342.
The Influence of Hypothalamic Stimulation on Intestinal Activity. J. H. Masserman and E. W. Haertig. 350.
On the Relationship between Choline Esterase and the Development of Behaviour in Amphibia. K. A. Youngstrom. 357.
Sensimotor Cortex, Nucleus Caudatus, and Thalamus Opticus. J. G. D. de Barenne and W. S. McCullough. 364.
Reflex Discharge from the Spinal Cord over the Dorsal Roots. J. F. Toennies. 378.

JOURNAL OF NERVOUS AND MENTAL DISEASE

Vol. 87. No. 1. January 1938.

The Emotional Factor in Skin Diseases. E. T. Bernstein. 1.
Further Experiences in the Insulin-Hypoglycemia Treatment of Schizophrenia. D. E. Cameron. 14.
Chronic Headache. P. A. Draper. 26.
Primary Melanomas of the Leptomeninges. M. T. Schnitker and D. Ayer. 45.
A Family with a Sex-Linked Hereditary Ataxia. E. V. Turner and E. Roberts. 74.

Vol. 87. No. 2. February 1938.

The Significance of the Convulsive Reaction during the Insulin and the Cardiazol Therapy of Schizophrenia. L. v. Meduna. 133.
On the Significance of the Epileptic Convulsion as a Therapeutic Factor in the Pharmacological Shock Therapy of Schizophrenia. M. Sakel. 140.
The Incidence of Pilonidal Sinuses in Mental Defectives. W. J. Johnson. 156.
Psycho-analytic Remarks on "Alice in Wonderland" and Lewis Carroll. P. Schilder. 159.
Mnemistic Biology and Psychology. E. Bleuler. 169.
The Relationship of the Segmental Nuclei of the Brain Stem. W. F. Allen. 202.

Vol. 87. No. 3. March 1938.

Measurement of Intelligence. T. Braatöy. 265.
The Clinical Significance of Lumbar Radiculitis and of Neuritis of the Femoral Nerve. J. B. Doyle. 283.
Language Study in Schizophrenia. W. L. Woods. 290.
A Study of Porencephaly. A. Laird. 317.
Spongioblastoma of the Diencephalon. M. G. Masten. 322.
The Rationale of Psychiatric Therapy. G. S. Sprague. 325.

Vol. 87. No. 4. April 1938.

Meningo-Encephalo-Myeloradiculitis. P. Goolker. 405.
Recurring Maculo-Popular Exanthems as Preludes to Marked Exacerbations in Myasthenia Gravis. L. F. Barker. 416.
Psychoses Among Followers of Father Divine. L. Bender and Z. Yarrell. 418.
Huntington's Chorea and Luetic Meningo-Encephalitis. T. T. Stone and E. I. Falstein. 450.
Comments on the Treatment of Drug Addiction with Protracted Narcosis. W. H. Chao, Y. K. Hsü, and R. S. Lyman. 454.
Upper Motor Neurone Sequelæ in "Jake" Paralysis. M. A. Zeligs. 464.

Vol. 87. No. 5. May 1938.

Is There a Relative Increase in Mental Disease? B. Malzberg. 545.
Blood Pressure and Pulse Rate in Prison Psychosis. R. Schwarz. 556.
Insulin in the Treatment of Acute Mania. L. C. Grosh. 559.
The Effect of Induced Metrazol Convulsions on Schizophrenic Patients. H. H. Reese, A. H. Vander Veer, and A. H. Wedge. 570.
The Psychological Effect of Benzedrine Sulphate. P. Schilder. 584.
Correlations of Athetosis, Catatonia, and Hypoglycemia. K. Gyárfás. 588.
Electroencephalography in the Diagnosis and Localization of Intracranial Conditions. T. J. Case. 598.

Vol. 87. No. 6. June 1938.

Hemidecortication in Chimpanzee, Baboon, Macaque, Potto, Cat, and Coati. A. E. Walker and J. F. Fulton. 677.
Studies of Neuropsychiatric Data in Relation to the Motion of Growth: the Insulin Hypoglycemia Therapy in Schizophrenia Viewed as an Induced Growth Process. D. E. Schneider. 711.
Parotid Secretory Rate in Schizophrenic Patients. E. I. Strongin and L. E. Hinsie. 715.
Tumors in the Tuberculum Sella. R. A. Groff. 725.

JOURNAL OF PHYSIOLOGY

Vol. 92. No. 4. May 1938.

Experimental Traumatic Shock. J. R. Bell, A. M. Clark, and D. P. Cuthbertson. 361.
Quantitative Data on the Inhibition of Œstrus by Testosterone, Progesterone, and Certain Other Compounds. J. M. Robson. 371.
Some Factors Influencing Venous Pressure in Man. J. Doupe, R. A. Krynauw, and S. R. Snodgrass. 383.
Antagonism between Progesterone and the Synthetic Œstrogenic Substance, Triphenyl Ethylene. J. M. Robson. 401.
The Effect of Adaptation of Differential Brightness Discrimination. K. J. W. Craik. 406.
Action of Hordenine Compounds on the Centra. Nervous System. A. Schweitzer and Samson Wright. 422.
The Respiration and Metabolism of Submaxillary Gland Tissue of the Cat. W. Deutsch and H. S. Raper. 439.
The Effect of Large Doses of Insulin on the Fœtal Sheep and Goat. R. Passmore and H. Schlossmann. 459.
Coughing Studied by Means of X-Ray and Cinematography. K. J. Franklin and R. Janker. 467.

Vol. 93. No. 1. June 1938.

The Role of Leucocytes in Fat Absorption. E. H. Leach. 1.
On the Mechanism of Production and the Physiological Significance of "Apneusis." G. Stella. 10.
The Thermal Decomposition of Visual Purple. R. J. Lythgoe and J. P. Quilliam. 24.
The After Effects of a Tetanus on Mammalian Muscle. G. L. Brown and U. S. v. Euler. 39.
The Influence of Anterior Pituitary Extracts, Injected either with or without Insulin, on the Glycogen Contained in the Livers of Fasting Young Rabbits. H. P. Marks and F. G. Young. 61.

Vol. 93. No. 2. July 1938.

The Carotid Sinus and Blood Regeneration. A. L. Latner. 75.
The Osmotic Pressure of Fœtal and Maternal Sera in the Sheep. E. F. McCarthy. 81.
The Transmission of Impulses by Ganglionic Direct Fibres. D. P. C. Lloyd. 86.
The Effect of Asphyxia upon the Heart Rate of Rabbits at Different Ages. D. J. Bauer. 90.
Segmental Distribution of Certain Visceral Afferent Neurones of the Pupillo-Dilator Reflex in the Cat. B. A. McSwiney and S. F. Suffolk. 104.
Carbonic Anhydrase Activity Inside Corpuscles. Enzyme-Substrate Accessibility Factors. V. H. Booth. 117.
Action of Adrenaline, Acetylcholine, and Other Substances on Nerve-Free Vessels (Human Placenta). U. S. v. Euler. 129.
The Effects of Prolonged Muscular Exercise on the Metabolism. J. N. Mills. 144.
The Action of Adrenaline in Accelerating the Removal of the Blood Sugar by the Peripheral Tissue. H. P. Himsworth, D. B. McN. Scott. 159.

MONATSSCHRIFT FÜR PSYCHIATRIE UND NEUROLOGIE

Vol. 99. Nos. 1–6. April 1938.

Über Epilepsie bei Hydrocephalus. (Epilepsy in cases of hydrocephalus.) E. Fünfgeld. 1.
Die Welt des Zwangskranken. (Psychology of compulsion neurosis.) V. E. v. Gebsattel. 10.
Spätform der amaurotischen Idiotie unter dem Bilde der Paralysis agitans. (Late form of amaurotic idiocy producing the clinical picture of paralysis agitans.) J. Hallervorden. 74.
Arzneimittel oder Arzneibehandlung. (Medicines or medication.) W. Heubner. 81.
*Über Thalamus- und Subthalamussyndrome und die Störungen einzelner Thalamuskerne. (Thalamic and subthalamic syndromes, and disturbances of single thalamic nuclei.) K. Kleist and J. Gonzalo. 87.
Hirnchirurgie und Lokalisationslehre (Hirnlappen- und Hemisphärenausschneidungen). (Neurosurgery and localization. Extirpation of lobes and hemispheres.) J. Lange. 130.
Die pathologische Synaps. (The pathological synapsis.) N. v. Mayendorf. 145.
*Zur Frage der somatotopischen Faktoren bei Hemiathetose. (Somatotopic factors in hemiathetosis.) H. Hoff and O. Pötzl. 170.
Stand und Entwicklung der Hirndrucklehre. (The theory of intracranial pressure.) F. Sauerbruch. 192.
*Riechstörungen und Hornersches Syndrom nach Kopftrauma. (Olfactory disturbances and Horner's syndrome after cranial injury.) E. Stier. 201.
Zur Frühdiagnose des Akustikustumors. (Early diagnosis of acoustic nerve tumour.) K. Vogel. 227.
Wandlungen des Hysteriebegriffes. (Historical development of the conception of hysteria.) R. Gaupp. 233.
Kinderpsychiatrie. (Child psychiatry.) P. Schröder. 269.
Über ein motorisches Krankheitsbild im Kindesalterl (A motor disease occurring during childhood.) F. Kramer. 294.
Schizophrenie und symptomatische Geisteskrankheit im Erbgesundheitsverfahren. (Schizophrenia, symptomatic psychosis, and law of sterilization.) H. Seelert. 300.
Weitere Beiträge zur Kenntnis des apoplektisch entstehenden Syndroms: Lachzwang bsw. Euphorie kombiniert mit Astereognosie. (Further contributions to the syndrome: Spastic laughter and euphoria combined with astereognosis.) H. Fabritius. 309.
Brompsychose mit ungewöhnlicher Wahnbildung. (Bromide psychosis with unusual delusions.) K. Pohlisch. 315.
Zur Kenntnis der kongenitalen Wortblindheit (angeborenen Lese-Schreibschwäche). (Congenital word-blindness.) R. Thiele. 371.
Über den Geltungsbereich und die Bedeutung des psychiatrischen Urteils. (Value and significance of psychiatric judgment.) J. Zutt. 399.
Die Bewusstseinstrübung bei symptomatischen Psychosen. (Dimming of consciousness in symptomatic psychosis.) G. Ewald. 411.
Der Fall Otto Velten. (Zur Psychopathologie der rezidivierenden Hyperkinesen.) (A case of recurrent hyperkinesis.) H. Schulte. 422.
Die allgemeine Pathologie der Entwicklung im Rahmen der morphologischen Hirnforschung. (General pathology of embryological development in relation to neuropathology.) B. Ostertagn 434.
*Über zwischenhirnabhängige Stoffwechselstörungebei Chorea Huntington. (Diencephalic disturb-

ances of metabolism in Huntington's chorea.) F. Panse. 448.
Krüppeltum, Erlebnis und Entartung bei der Paranoia. (Disability, experience, and degeneration in paranoia.) W. Betzendahl. 473.
*Über den Nachweis von Geschwulstzellen im Liquor cerebro-spinalis. (Tumour cells in the C.S.F.) H. G. Creutzfeldt and R. Riebler. 488.
Zwei Fälle von Psychose bei Tetanie. (Two cases of psychosis in tetany.) H. Knospe. 503.
Hypoglykämische Anfälle bei Inselzelladenom mit Ausgang in hyperglykämisches Koma. (Adenoma of the pancreas producing hypoglycæmic attacks, finally leading to hyperglycæmic coma.) H. Scheller and F. Stroebe. 520.
*Über vorläufige Erfahrungen bei der Behandlung der tabischen Opticusatrophie mit der Entlastungstherapie nach Sobanski. (Treatment of tabetic optic atrophy according to Sobanski.) C. Aumann, A. Brüning, and H. Sohr. 532.
Zum Problem der Commotio cerebri. (Cerebral concussion.) E. Gamper. 542.

Thalamic and Subthalamic Syndromes.—Two cases are described clinically and anatomically. The first case showed the syndrome of the rubro-thalamic artery, the second case showed the syndrome of Foix' thalamo-geniculate artery. Lesion of the n. ruber produced disturbance of posture of the contra-lateral head, trunk, and arm. Lesion of the ventral thalamic nucleus and subthalamic formations (corpus subthalamus, red nucleus, substantia nigra) produced intention tremor and ataxia. Circumscribed lesion of the posterior ventral nucleus produced a circumscribed sensory disturbance. Both cases suffered from spontaneous unpleasant sensations (pain and temperature). Emotional disturbances are explained by the lesions of medial nuclei. Spastic crying is explained by lesion of the centre median or by bilateral lesion of the anterior segment of the internal capsule. Disturbance of consciousness is, according to the authors, due to lesions of the central grey matter and massa intermedia. (K. S.)

Hemiathetosis.—In a case of a localized athetosis of the four ulnar fingers of one hand autopsy revealed a tubercle occupying the homolateral dentate nucleus, its hilus, and the most oral quarter of the tegmentum of the pons, and the superior peduncle up to the decussation. Another small tubercle was found in the head of the caudate nucleus on the contralateral side. (K. S.)

Olfactory Disturbance and Horner's Syndrome.—Twelve cases are described clinically. Simple unilateral or bilateral anosmia is mostly due to lesions of the olfactory bulbs. Symptoms of the neighbourhood are: mental symptoms due to frontal lobe lesions, Horner's syndrome due to lesion of the carotic plexus (three cases), disturbances of taste, reflex differences, and sensory disturbances. Olfactory hallucinations are explained by cortical lesions. In only one case parosmia combined with an intact sense of smell was observed. This is possibly explained by a lesion of the insula. (K. S.)

Huntington's Chorea.—Nine families with Huntington's chorea showed frequent occurrence of diabetes. In one case both diseases occurred in the same individual. Psoriasis also occurred more frequently than in the average population; in several cases the patient's brother or sister or daughter suffered with psoriasis. (K. S.)

Tumour Cells in the C.S.F.—It is shown that a method first described by Alzheimer is considerably better for the demonstration of tumour cells in C.S.F. and cyst fluids than the simple stained smear preparations. (K. S.)

Tabetic Optic Atrophy.—According to Sobanski the diastolic pressure in the central retinal artery is abnormally low in the majority of cases of tabetic optic atrophy. The intraocular pressure is often higher than normally. These two factors are regarded as important for the pathogenesis of the disease. Therefore Sobanski proposed to lower the intraocular pressure by "cyclodialysis" (operative procedure which has been successfully applied against glaucoma) and following pilocarpine treatment. The authors tried this procedure in 30 patients. In six cases the visual fields were slightly improved. In three cases they became smaller after the treatment. Visual acuity improved very slightly in seven cases, and became worse in seven cases. (K. S.)

PHYSIOLOGICAL REVIEWS

Vol. 18. No. 3. July 1938.

The Physiological and Pathological Aspects of Silica. E. J. King and T. H. Belt. 329.
The Rôle of Inflammation in Immunity. V. Menkin. 366.
Hormones and the Placenta. W. H. Newton. 419.
Pharmacology of the Anesthetic Gases. M. H. Seevers and R. M. Waters. 447.

PSYCHIATRIC QUARTERLY

Vol. 12. No. 3. July 1938.

*Improvement and Recovery Rates in Dementia Præcox without Insulin Therapy. D. Whitehead. 409.
*"Spontaneous" Remissions in Dementia Præcox. R. C. Hunt, H. Feldman, and R. P. Fiero. 414.
Some Comparisons between Insulin-Treated and

Non-Insulin-Treated Cases of Schizophrenia. R. A. Savitt. 426.
Statistical Comparisons Between Preinsulin and Insulin Eras. J. Notkin and F. J. DeNatale. 432.
Insulin Therapy and Its Complications in the Treatment of the Psychoses. O. J. McKendree. 444.
Serious Complications of Insulin Shock Therapy F. J. O'Neill. 455.
Protracted Comas Occurring During Insulin Hypoglycemic Therapy. W. A. Horwitz, J. R. Blalock and M. M. Harris. 466.
Prolonged Coma in the Insulin Treatment of Dementia Præcox. R. F. Binsley and J. L. Anderson, 477.
Further Metabolic Studies Regarding the Effect of Insulin Hypoglycemic Therapy in Mental Patients. M. M. Harris, J. R. Blalock, and J. L. Anderson. 489.
Studies in Parotid Secretion of Patients Before, During, and After Insulin Hypoglycemic Therapy. E. I. Strongin, L. E. Hinsie, and M. M. Harris. 506.
The Mechanism Underlying the Low Rectal Temperature in Hypoglycemia. H. S. Barahal. 514.
*Outcome of Insulin Treatment of One Thousand Patients with Dementia Præcox. B. Malzberg. 528.
Status of Paroled Patients Treated with Hypoglycemic Shock. D. M. Carmichael. 554.
*Prognosis in Dementia Præcox. J. A. Taylor and C. V. von Salzen. 576.
The Interpersonal Content in Schizophrenic Thought. H. K. Johnson. 583.

Recovery in Dementia Præcox without Insulin.—In this paper an attempt has been made to provide a study of control cases with a view to evaluating the efficacy of insulin treatment of schizophrenia. Ninety consecutive cases of dementia præcox entering the Utica State Hospital were studied. The admissions were in the fiscal year 1935–36 and the survey was made in January 1937 allowing from 6 to 18 months' observation of each case. None of the cases had been treated by insulin. Of these 90 cases 9 recovered completely, 7 improved greatly, 20 improved, and 62 showed no improvement. When the cases were classified as to the duration of the psychoses it was found that: Under 6 months, improvement took place in 50 per cent. and 22 per cent. recovered. From 6 to 18 months 38 per cent. improved with no recovery. Over 18 months improved in 23 per cent. with no recovery.

Another survey was made of 105 consecutive admissions of dementia præcox cases during the fiscal year 1931–2. None of the cases were treated with insulin. The diagnoses were changed in three cases leaving 102 cases to be considered. Again classifying the cases according to the duration of the psychoses, it was found that when the duration was under 6 months improvement occurred in 61 per cent. with 5 per cent. recoveries. From 6 months to 2 years improvement in 61 per cent. with no recoveries took place. Over 2 years' duration there was a 30 per cent. improvement with no recoveries. Thus in the survey of 102 consecutive cases of dementia præcox 5 years after admission, 51 per cent. improved, 27 per cent. were much improved, and 2 per cent. recovered.

Spontaneous Remissions in Dementia Præcox.—The material for this study consisted of the case records of 677 consecutive first admissions diagnosed as dementia præcox. These cases were admitted to the Rochester State Hospital between July 1927 and June 1934. For various reasons 36 of these cases were discarded from the statistical study. None of these cases had received any insulin treatment. In 101 catatonics 41·6 per cent. were much improved and 12·9 per cent. improved. In 151 hebephrenics 19·2 per cent. were much improved and 20·5 per cent. improved. In 218 paranoias 10·5 per cent. were much improved and 19·3 per cent. improved. In 161 cases of less than 6 months' duration 35·4 per cent. were much improved and 19·2 per cent. improved. In 150 cases of 6 to 18 months' duration 18·6 per cent. were much improved and 16·7 per cent. improved. In 330 cases of over 18 months' duration 10 per cent. were much improved and 15·4 per cent. improved. In all the 641 cases, 18·4 per cent. were much improved and 16·7 per cent. improved. The remissions developed on an average of 9·5 months after admission.

Insulin Treatment of Dementia Præcox.—This study is based on the histories of 1,039 patients with dementia præcox who were treated with insulin in several civil state hospitals. Of the 1,039 patients 12·9 per cent. were reported as recovered at the end of the treatment; 27·1 per cent. were much improved; and 25·3 per cent. were improved. 33·4 per cent. showed no improvement. Thirteen patients died during treatment. Rates of recovery and improvement varied widely in the several hospitals. The control group consisted of 1,039 first admissions with dementia præcox, almost all of whom were admitted during the year July 1st, 1935, to July 1st, 1936. Each patient in the control group had thus been under observation for at least 1 year, and most patients had been observed for 2 years. Of the control group, 3·5 per cent. were described as recovered, 11·2 per cent. as much improved, and 7·4 per cent. as improved. The paper includes a number of statistical tables dealing with the various correlations of the results of treatment.

Prognosis in Dementia Præcox.—The suitability of a dementia præcox patient to be given parole and the ability to complete successfully a full year on parole were the objective criteria used in this study of the prognosis of schizophrenia. The result of treatment was assessed on the ability of the patient to return home on parole and remain there for a year. 15 per cent. of such patients made a good remission, 38 per cent. a fair remission, and 47 per cent. either made a poor remission or were returned to hospital before the completion of 1 year on parole. Insulin therapy was completed in 74 cases and

there was a control group of 638 cases. 62 per cent. of the 40 insulin treated patients who had suffered from dementia præcox for less than 2 years could be put on parole whilst in a control group of 638 cases with symptoms of similar duration, 54 per cent. were paroled. The authors consider that the quality and duration of the remissions in the two groups of cases must be studied before they can pronounce on the value of the insulin treatment at King's Park State Hospital.

REVUE NEUROLOGIQUE

Vol. 69. No. 5. May 1938.

*Sur l'Idiote Amaurotique Juvénile. (Juvenile amaurotic idiocy.) G. Marinesco. 449.

Le Complexe Épithalmo-Épiphysaire. (The epithalamo-epiphyseal system.) G. Roussy and M. Mosinger. 459.

*Des Hématomes Sous-Duraux. (Sub-dural hæmatomata.) Riser, Ducuing, and Géraud. 471.

*De la Sclérose en Plaques Chez l'Enfant. (Disseminate sclerosis in a child.) L. Rimbaud, Riser, and Géraud. 477.

Juvenile Amaurotic Idiocy.—A discussion by the author of the various classifications and the pathology of the amaurotic idiocies. (E. A. C.)

Sub-Dural Hæmatomata.—Description of a case in which hæmorrhages were also found in the pons and peduncles. (E. A. C.)

Disseminate Sclerosis in a Child.—Three cases are described clinically in which the diagnosis was made. No pathological studies were available. (E. A. C.)

Vol. 69. No. 6. June 1938.

*Reconnaissance et Contrôle des Troubles Pupilaires Utilisables en Sémiologie et Neurologie. (Recognition and control of pupillary disturbances occurring in neurology.) Bollack and Monbrun. 590.

*Valeur Sémiologique et Diagnostique des Troubles Pupillires dans les Affections Neurologiques d'Ordre Médical et Neuro-Chirurgical. (Semiological and diagnostic value of pupillary abnormalities in neurological and neurosurgical conditions.) Velter and Hartmann. 629.

*Recherches d'Explications Physiopathologiques. (Physiopathological investigations.) M. Tournay. 707.

The above articles with others are the main addresses given at an international symposium. They are too long to abstract. Much valuable information is contained in them. (E. A. C.)

Vol. 70. No. 1. July 1938.

L'Hémiballisme et le Corps de Luys. (The relationship of acute hemichorea to the body of Luys.) H. Marcus and H. Sjögren. 1.

La Méralgie Paresthésique au Cours de l'Anévrisme de l'Aorte Abdominale. (Meralgia paræsthetica in the course of aneurysm of the abdominal Aorta.) A. de Castro. 29.

Rôle des Solutions Hypertoniques dans le Traitement de la Migraine. (The effect of hypertonic solutions in the treatment of migraine.) G. Villey, J. F. Buvat, and Buvat-Pochon. 32.

RIVISTA DI NEUROLOGIA (NAPOLI)

Vol. 11. No. 2. April 1938.

*La Reazione di Donaggio nell' Epilessia. (Donaggio's reaction in epilepsy.) P. Jedlowski. 89.

*Sindromi Neurologiche da Intossicazione Emetinica. (Neurological syndromes from emetine poisoning.) F. Vizioli. 145.

*Sulla Presenza della Rete Neurofibrillare Endocellulare di Donaggio nelle "Cellule Vescicolose" del Mesocefalo. (On the presence of the neurofibrillary net of Donaggio in the vasicular cells of the messencephalon.) P. Jedlowski. 160.

Il Problema delle Allucinazioni all'XI Congresso Internazionale di Psicologia. (The problem of hallucination discussed at the 11th International Congress of Psychology.) M. Gozzano. 166.

Donaggio's Reaction in Epilepsy.—Donaggio's precipitation reaction, due to the abnormal amounts of colloids in the urine and cerebrospinal fluid, has been investigated in epilepsy. The reaction is positive or if previously positive increased immediately after the fit. The maximum reading is generally found from 12 to 24 hours, though sometimes it occurs in 6 hours and sometimes as late as 42 hours. The intensity of the reaction on Donaggio's scale is on the average 33, sometimes being as high as 45 to 51. In 88 cases the direction of the reaction was on the average 106 hours with a minimum of 42 and a maximum of 192. If the test is done at frequent intervals each patient shows a similar curve of intensity and duration for his fits which differ from the curves of other patients. Cardiazol convulsions produce a positive reaction, but it is much less intense and lasts a much shorter time than a true epileptic fit. Unless the fits are very prolonged hysterical convulsions produce no reaction and even if present in such prolonged attacks it is feeble and of short duration. (R. G. G.)

Emetine Poisoning.—A brief review of the literature is given and two cases described. One, which had a very prolonged treatment, showed a polyneuritis of Dejerines pseudo-tabetic type, and the other, which had a maximal dose by the intravenous route, developed a spastic paraparesis. (R. G. G.)

Vesicular Cells of Mesencephalon.—The author shows that with the superior staining properties of Donaggio's method the neurofibrillary network in the primitive "vesicular" cells of the mesencephalon extends throughout the cell and into the axis cylinder and is not localized as was stated by Dide and Bauduin. (R. G. G.)

Vol. 11. No. 3. June 1938.

*Il Problema del Parkinson Traumatico. (The problem of traumatic Parkinsonism.) F. Vizioli. 185.

*Tubercoloma Midollare Mascherato da Mielite Necrotica. Aspetti Istologici della Necrosi Midollare. (A medullary tuberculoma masked by a necrotic myelitis.) G. Glück and B. Garau. 219.

La Scoliosi Spasmodica nella Diagnosi Differenziale fra Lombo Ischialgie Sintomatiche di Compressione della Coda Equina e Lombo Ischialgie Protratte Idiopatiche. (Spasmodic scoliosis in the differential diagnosis of lumbo sacral (sciatic) pain symptomatic of compression of the cauda equina and protracted lumbo sacral (sciatic) pain.) C. Masci. 247.

Traumatic Parkinsonism.—The author describes three cases of uncomplicated Parkinsonism following cranial injury. All three cases had suffered from epidemic encephalitis and the trauma had precipitated the Parkinsonian syndrome, but in the author's opinion was not the primary cause. It is argued that the morbid anatomy of the syndrome and in fact all considerations in relation to it makes it exceedingly unlikely that any cranial trauma and especially a peripheral cranial injury could be truly causal. (R. G. G.)

Medullary Tuberculoma.—The clinical and pathological characteristics of the case are described and the rarety of a single tuberculoma is remarked. In this case the transverse myelitis occurred at some distance from the tuberculoma and apparently quite independently of it. It entirely masked the latter, which was not suspected during life. The way in which a single tuberculoma arises in the cord presumably from a focus of infection outside the nervous system is discussed. (R. G. G.)

RIVISTA DI PATOLOGIA NERVOSA E MENTALI

Vol. 51. No. 2. March 1938.

*Paralisi Progressiva ed Endemia Malarica. (Progressive paralyses and endemic malaria.) V. Desogus. 179.

*Sull' Encefalomielopatia Sperimentale da Cianuro di Potassio. (On experimental lesion of brain and spinal cord induced by cyanide of potassium.) P. Jedlowski. 231.

*Ulteriori Dati per la Conoscenza della Base Anatomica delle Modificazioni Funzionali Reversibili del Nervo Ottico nell' Intossicazione da Chinino. (Further data in the knowledge of the anatomical basis of the reversible functional changes in the optic nerve in quinine intoxication.) P. Jedlowski. 276.

*Anatomia Patologica della Ployradiculitis Acuta Curabilis con Dissociazione Albumino-Citologica : Sindrome di Guillain-Barré. (The pathological anatomy of the syndrome of Guillain-Barré's acute curable polyradiculitis with dissociation of albumen and cell count in the C.S.F.) O. Balduzzi. 288.

*Sulla Polinevrite Acuta Febbrile. (On acute febrile polyneuritis.) V. Longo. 313.

*La Prova del Somnifen in Semiologia Nervosa. (The somnophane test in the symptomatology of nervous disease.) O. Balduzzi. 337.

Progressive Paralyses and Endemic Malaria.—The important question as to whether endemic malaria protects the population from general paralysis is examined especially in relation to the malaria infested island of Sardinia. The author concludes definitely that endemic malaria is not associated with diminution of incidence of general paralyses. Endemic malaria is generally associated with a low grade of civilization and in such regions syphilis may spread more readily and be treated less efficiently. But, however, such considerations and the question of the dermotropism of the spirochæte in lower grades of culture and its neurotropism in higher grades complicate the statistical records, the conclusion that the fact of having had malaria does not protect from G.P.I. is not affected. (R. G. G.)

Brain and Spinal Cord Lesion Induced by Potassium.—Parenteral administration of potassium cyanide will produce disseminated demyelinating lesions of white matter throughout the nervous system. Donaggio's technique shows the stages through which the degenerated areas pass. These resemble the lesion of Schilders' disease and the author suggests that this represents one of the rare occasions on which experimental lesions in animals and acquired human disease are identical. (R. G. G.)

Optic Nerve Changes in Quinine Intoxication.—The ambliopia and blindness which may occur when quinine hydrochloride is administered is due to primary degenerations of the nerve fibres which may be demonstrated by Donaggio's technique and is not due to secondary effects induced by vascular changes. The initial stage of

the primary degeneration is reversible. (R. G. G.)

Pathological Anatomy of Guillain-Barre Syndrome.—A typical case suddenly died when she was beginning to get better. The only lesion discoverable in the nervous system was in the roots especially in the lumbar region, the anterior being affected as much as the posterior. There was no indication of inflammation, but only a noteworthy vascular congestion which resulted in rupture of the neighbouring capillaries with small extravasations of blood. This would explain the flaccid paralysis without atrophy, the only partial loss of sensation, the spontaneous disappearance of all symptoms, and the dissociation of albumen and cell increase. It is unlikely to be due to a neurotropic virus, but may be an allergic reaction such as possibly may explain a post-diphtheritic neuritis. (R. G. G.)

Acute Febrile Polyneuritis.—A case with a complete post-mortem examination is presented. The main incidence of the lesion is on the peripheral nerves, but changes also occur in the grey matter of the spinal medulla and of the cranial nerve nuclei. These changes are not severe and are limited to single cells. In this case, in contrast to those of other authors, the alterations were of a degenerative and not of an inflammatory type. A very comprehensive survey of the literature is given with the object of separating acute febrile polyneuritis from other infections of the nervous system. (R. G. G.)

Somnophane Test in Symptomatology of Nervous Disease.—The author claims that if 3·3 c.c. dissolved in 10 c.c. of distilled water is slowly injected intravenously it is possible to demonstrate much more minute differences especially in sensibility but also of motor power and reflex activity between the two sides than can be shown without the injection. If therefore there is a lesion in a silent area it may be possible to localize it. He thinks this may be useful not only in cerebral tumours but also in Parkinsonianism and other extrapyramidal lesions, but also perhaps in the psychoneuroses. (R. G. G.)

SCHWEIZER ARCHIV FÜR NEUROLOGIE UND PSYCHIATRIE

Vol. 41. No. 1. 1938.

*Über familiares Auftreten von Zwergwuchs und Epilepsie bei Zwischenhirnstörung. (Familial dwarfism and epilepsy combined with disturbance of the diencephalon.) O. Billig. 1.

Weitere Beobachtungen nach Rorschach's Testmethode. (Further observations on Rorschach's test.) A. Guirdham. 8.

*Hirnverletzung und Schizophrenie. (Cerebral injury and schizophrenia.) E. Feuchtwanger and W. Mayer-Gross. 17.

*Klinische Erfahrungen an 50 mit der Konvulsionstherapie nach L. v. Meduna behandelten Schizophrenen. (Experiences with 50 cases of schizophrenia treated with cardiazol.) W. Meier. 100.

*Psychologische Grundlagen zum Delikt des Mords und Totschlages. (The psychology of murder and manslaughter.) P. Mohr. 135.

Contribution à l'Étude de la Physio-Pathologie du Liquide Cephalo-Rachidien au Cours du Traitement Insulinique de la Schizophrenie. (The cerebrospinal fluid during insulin treatment.) T. A. Ott. 157.

*Untersuchungen zum Übertritt von Alkohol in die Cerebrospinalflüssigkeit. (Alcohol in the C.S.F.) F. N. Riklin. 173.

*Zur Frage der zentralen Umstimmung der Sehschärfe peripherer Netzhautbezirke. (Cerebral influence on the visual acuity of peripheral areas of the retina.) F. Singeisen. 193.

Experimentalle Untersuchungen betreffs der Psychogenese der essentiellen Hypertension. (Experiments on the psychogenesis of genuine hypertension.) B. Stokvis. 200.

Familial Dwarfism and Epilepsy.—A patient with chondrodystrophia, obesity, and hypogenitalism developed Alzheiner's disease and epileptic attacks at the age of 57. The same syndrome or parts of it could be observed in several members of the same family in four generations. (K. S.)

Cerebral Injury and Schizophrenia.—1,554 cases of cerebral injury from the war form the basis of this investigation. The total percentage of schizophrenia and symptomatic psychoses of schizophrenic character was more than four times as high as in the average population. True schizophrenia, however, was not more frequent than in the average population. There was no relation between localization and severity of the cerebral lesion on one side and the psychosis on the other. The single case reports, especially the various relations between symptomatic epilepsy and schizophrenic psychosis, are most interesting, but cannot be abstracted in detail. (K. S.)

Schizophrenia treated with Cardiazol.—In 14 cases there was a full recovery which lasted to the time of this report (on the average 6½ months). Of 10 cases in which the psychosis had lasted for less than 6 months, 9 showed a complete recovery. In cases of a duration of more than 3–4 years, recovery cannot be expected. In almost every case, however, the treatment had a transient symptomatic effect. (K. S.)

Psychology of Murder and Manslaughter.—In 51 cases relatives of the criminals had already committed crimes. The cases are grouped according to the motivation of the crime. (K. S.)

Alcohol in the C.S.F.—Alcohol was given by mouth, and its concentration estimated in intervals of 10–20 minutes in the blood,

lumbar, and cisternal fluid. The concentration of alcohol in the cisternal fluid is more parallel to that in the blood than is the concentration in the lumbar fluid. The first symptoms of intoxication (the tested persons were patients with G.P.I. or schizophrenia !) were observed after 43 minutes, when the concentration in the blood was 0·099 per cent., in the cisternal fluid 0·085 per cent., in the lumbar fluid 0·045 per cent., and disappeared again after 160 minutes, when the concentration in the blood was 0·080 per cent., in the cisternal fluid 0·099 per cent., and in the lumbar fluid 0·095 per cent. (K. S.)

Cerebral Influence on Visual Acuity.—In a patient with infarction of the retina due to embolism of the central retinal artery a small area in the upper temporal quadrant was preserved, owing to a rare anastomosis from a cilio-retinal vessel. During monocular vision this eye could only perceive a faint glimmer. During binocular vision with fixation double vision occurred, the distinct second picture being perceived by the diseased eye. This observation is in favour of Potzl-Goldstein's theory of the central influence on the visual acuity of the retina. (K. S.)

ZEITSCHRIFT FÜR DIE GESAMTE NEUROLOGIE UND PSYCHIATRIE

Vol. 162. Nos. 1 and 2. March 1938.

Die epileptiformen Anfälle der Schizophrenen und die differentialdiagnostischen Schwierigkeiten im Grenzgebiet von Epilepsie und Schizophrenie. (Epileptiform fits in schizophrenics and the difficulties of differential diagnosis in the borderland between epilepsy and schizophrenia.) P. H. Esser. 1.

Schizophrenie und Tuberkulose. (Schizophrenia and tuberculosis.) C. H. Alström. 25.

Das Gebiet der Perseverationen. (The province of perseveration.) E. Roenau. 51.

*Zur Psychopathologie der hypoglykämischen Zustände bei Schizophrenen. (Auf Grund von Beobachtungen während der Insulintherapie.) (The psychopathology of the hypoglycæmic state in schizophrenics. Observations during insulin therapy.) A. Erb. 65.

Ergebnisse einer siebten Messungsserie zur Frage des Zusammenhangs zwischen Radioaktivität und Kropf. (The results of a seventh series of measurements on the relations between radioactivity and goitre.) T. Lang. 72.

*Zur Frage cerebraler Kreislaufstörungen nach Hirntumoroperationen. (Disturbances of cerebral circulation after operations for brain tumour.) O. Kaufmann. 89.

Über die otogene Encephalitis purulenta progressiva. (Otogene Encephalitis phlegmonosa.) (Otogenous progressive purulent encephalitis. Otogenous phlegmonous encephalitis.) H. Brunner and R. Dinolt. 106.

Ein Fall von reinem Hemiballismus auf dem Boden eines degenerativen Nervenleidens. (A case of pure hemiballismus with an underlying degenerative nervous disorder.) C. Baumann. 126.

Die Behandlung der postencephalitischen Schauanfälle von Calcibronat. (The treatment of postencephalic oculogyric crises with calcibronat.) F. Duensing and L. Meyer. 136.

Über Volumänderungen des Gehirngewebes in Pufferlösungen verschiedener *p*H. (Alterations in the volume of brain tissues in buffer solutions of various *p*H.) H. Selbach. 145.

Experimentelle Untersuchungen über die durch Reizung des Zwischen-und Mittelhirns hervorgerufenen assoziierten Augenbewegungen. (Experimental researches on the production of associated eye movements by stimulation of the between-brain and midbrain.) W. Godlowski. 160.

Zur Erblichkeit der Ischias. (Zwillingsstudien über die Erbanlage bei der Neuritis lumbosacralis.) (Heredity of sciatica. Studies in twins of the hereditary basis of lumbosacral neuritis.) P. E. Becker. 183.

Zur Pathologie des Raumerlebens, unter besonderer Berücksichtigung des Sehraums. (The pathology of spatial awareness with some considerations of visual space relations.) F. Laubenthal. 202.

Myatonia congenita (Oppenheim) bei eineiigen Zwillingen. Neurologische Zwillingsstudien 2 Mitteilung. (Myatonia congenita of Oppenheim in uniovular twins. Neurological twin studies part 2.) K. Thums. 233.

*Über die Gliaverhältnisse des Nucleus dentatus und der Olive. (The glia ratio in the nucleus dentatus and olive.) Fr. Tebelis. 252.

Parallelismen in elektro-biologischen Vorgängen der Hirnrinde bei pathopsychologischen und parapsychologischen Erscheinungen. (The parallelism of electro-biological processes in the cortex with pathopsychological and parapsychological phenomena.) L. J. Franke and L. J. Koopman. 259.

Beitrag zur Frage des Heiratskreises der Schizophrenen. Demographische und psychiatrische Untersuchungen in der engeren biologischen Familie von Ehegatten Schizophrener. (The question of the marriage circle of schizophrenics, a demographic and psychiatric study of the close biological family of married schizophrenics.) P. Leistenschneider. 289.

Über die Möglichkeit des Auftretens von Kinderreihen mit Schizophrenen unter der Nachkommenschaft Schizophrener. (The possibility of the appearance of a succession of schizophrenic children in the descendants of a schizophrenic.) B. Schulz. 327.

Hypoglycæmic States in Schizophrenia.—The author studies the temporary amelioration of mental symptoms under the influence of the hypoglycæmic state in insulin treatment. There is an immediate reaction which occurs near the beginning of the treatment in which the improvement is of short duration and only during the hypoglycæmic period. The late reaction occurs later in the treatment, lasts longer, and is present apart from the hypoglycæmic state. He uses this as a criterion of possible recovery, and finds that the best remissions occur when the immediate reaction appears soon (in three or four days), lasts longer, and recurs with nearly every insulin injection. (G. M. G.)

Disturbances of Cerebral Circulation after Brain Operations.—Seven cases are discussed where death follows soon after operative interference for brain tumour. In these softenings or hæmorrhages have occurred distant from the tumour in a region with a different vascular distribution. These lesions are caused by the abnormal reaction of the circulatory system. The

disturbances are not necessarily lethal, and may be reversible, depending on the topography and intensity of the reaction. (G. M. G.)

Glia Ratio in Dentate Nucleus.—A study of the types of glial cell found in the dentate and olivary bodies in the brains of executed persons and those dying of bodily disease with normal brains shows that there are variations in the type of cell in both areas. In some cases there was found a difference in the glia between the regions of the neo- and paleocerebellar dentate. In some brains there was a difference in type of cell in the dorsal and ventral parts of the olive. The author thinks that the variations have a constitutional basis and are independent of age or type of illness. (G. M. G.)

Vol. 162. No. 3. April 1938.

Beitrag zur einer schwäbischen Stammespsychopathologie. (A contribution to the psychopathology of the Schwabian people.) H. G. Weitbrecht. 343.

*Über cerebrale Endarterien. (Cerebral end-arteries.) E. Scharrer. 401.

Nanosomia pituitaria hypoplastica hereditaria. (Hereditary hypoplastic pituitary infantilism.) W. Dzierżynski. 411.

Koloquinten-Polyneuritis. (Colocynth polyneuritis.) F. W. Kroll. 422.

Ein Beitrag zur Kenntnis der Neurofibromatose (Recklinghausensche Krankheit). (A contribution to the study of neurofibromatosis. Recklinghausen disease.) E. Beck. 426.

Empfindung und Vorstellung im Seh-und Hörbereich. (Sensation and image in the realm of seeing and hearing.) O. Goebel. 443.

Psychopathologie des Traumes bei Schizophrenen und organischen Psychosen. (The psychopathology of dreams in schizophrenic and organic psychoses.) M. Boss. 459.

Zur Frage solaraktiver Einflüsse auf die Psyche. (The problem of solar influence on the psyche.) B. Düll and T. Düll. 495.

Cerebral End-Arteries.—A study of the vascular system of the American opossum shows that end-arteries only are present throughout the brain. They do not end strictly in the midline, but may pass over it, and the angio-architectonics do not entirely correspond to the cytoarchitectonics. (G. M. G.)

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Studien über den Vitamin C-Gehalt im Liquor cerebrospinalis. 5 Mitteilung. Der Einfluss von Narkose auf den Vitamin C-Gehalt im Liquor. (Studies in the vitamin C content of the C.S.F. Part 5. The influence of narcosis on the vitamin C content of the C.S.F.) M. Kasahara and I. Gammo. 673.

Brain Swelling.—The volume enlargement, brain swelling, is found in several conditions—uræmia, status epilepticus, toxic states, and as pseudo-tumour or with tumours. Dehydration methods may clear up the symptoms due to the swelling, while fluids by mouth or otherwise may precipitate the condition. Histological study shows that urea plays a part in the production of brain swelling, as demonstrated by crystals formed in sections treated by a xanthydrol method. These crystals were found in 27 cases of brain swelling from various causes, also in experimental states produced by electrical and other means. It is a physico-chemical problem of the relation of protein to the water absorbtion, the possible production of urea from brain proteins is considered. (G. M. G.)

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*Studien zur Pathologie der Hirngefässe. 1. Fibrose und Hyalinose. (Studies in the pathology of brain vessels. 1. Fibrosis and hyaline change.) W. Scholz and D. Nieto. 675.

*Studien zur Pathologie der Hirngefässe. 11. Die drusige Entartung der Hirnarterien und-capillaren. (Eine Form seniler Gefässerkrankung.) (Studies in the pathology of brain vessels. 11. Plaque-like

degeneration of brain arteries and capillaries. A form of senile vascular degeneration.) W. Scholz. 694.

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Formveränderungen der überlebenden Nervenzelle infolge Änderung der H-Ionkonzentration. (Alterations in the form of surviving nerve cells after changes of H ion concentration.) S. Huszák. 789.

Zur Periodik des manisch-depressiven Irreseins. (The periodicity of manic-depressive psychoses.) E. Slater. 794.

Das Weltmannsche Koagulationsband in der psychiatrischneurologischen Diagnostik. (The Weltmann coagulation band in psychiatric and neurological diagnosis.) F. K. Redlich. 802.

Kritisches und Experimentelles zur Deutung der Potentialschwankungen des Elektrocorticogramms. (A critical and experimental study of the interpretation of fluctuation of potential of electrocorticograms.) J. G. Dusser de Barenne and W. S. McCulloch. 815.

Pathology of Brain Vessels, Fibrosis, and Hyalinosis.—A discussion of hyaline fibrous and collagen changes in brain vessels. The hyalin change in the wall of smaller arteries is found between the elastica interna and the intima and shows as a yellow homogenous area with van Gieson stain; fat stains show red colour in the outer parts. The condition is associated with arteriosclerosis. (G. M. G.)

Pathology of Brain Vessels, Plaque-like Degeneration.—In brains of old people changes were found in the larger arteries consisting of a rhythmic ring-like thickening with a crystalloid, doubly-refracting substance, having the staining reactions of senile plaques. The crystalloid substance sometimes forms a plaque in the degenerated muscular coat or outside the vessel wall. The change was also found in capillaries. It was found mostly in the cerebral cortex and less in the cerebellia cortex and a little in the striatum, but none in the vessels of the white matter. The change was found in 12 per cent. of senile brains, and may form the bases of senile plaques. (G. M. G.)

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Cerebellopontine Angle Signs produced by Ependymomata. (Cyst, Tumour.) J. Hardman and G. Jefferson. 137.

*Atrophie optique primitive par méningiome à distance de la région opto-chiasmatique. (Primary optic atrophy due to Meningiomata situated at a distance from the optic chiasma.) C. Vincent, E. Hartmann, J. Le Beau. 145.

Zur Frage der Varices spinales und ihrer operativen Therapie. (The varicose veins of the spinal cord and their operative treatment.) L. Puusepp. 158.

*Hirngeschwulst und Lebensalter. (Cerebral tumours and age.) G. Schaltenbrand. 169.

Die angiomatösen Gewächse der Wirbelkörper. (The angiomatous growths of the vertebral bodies.) E. Koch-Grünberg. 188.

Lokalisierte bioelektrische Ableitungen von der Hirnrinde bei experimentellen Störungen des Blutkreislaufs des Gehirns. I. Abklemmung der Carotis communis. (Localized bioelectric recordings from the cerebral cortex during experimental disturbances of the blood circulation of the brain. I. Ligation of the common carotid.) A. Asenjo. 198.

*Über epileptische Anfälle beim Tumor cerebri. (Epileptic attacks associated with cerebral tumour.) O. Pedersen. 204.

Primary Optic Atrophy.—Primary optic atrophy associated with increased intracranial tension invariably suggests that the region of the optic chiasma is being directly compressed. The authors have recently seen two cases in which this syndrome was produced by meningiomata situated at some distance from this region. One was in the rolandic area, the other in the occipital lobe. The possible mechanisms responsible for this syndrome in these two cases are discussed. It is remarkable that in both cases visual disturbances were the first symptoms of the disease. (G. J.)

Cerebral Tumours and Age.—An investigation of 250 tumours forms the basis for a stimulating discussion of the relationship which exists between the histological characteristics of tumours, their place of origin, and the age of the patient. A formal division of cerebral growths into static groups is found to be both difficult and unsatisfactory. Investigation of different parts of the same tumour will reveal transitional characters belonging to more than one type. The anatomical study of the nervous systems of members of one family who succumbed to von Recklinghausen's disease at different age periods leads the author to express the view that most cerebral tumours are congenital and become evident when they have been stimulated to growth. A life-cycle of tumours is suggested during which their characters may undergo fundamental changes, and the parallelism of the ageing of the individual with changes in the tumour is pointed out. (J. S.)

Epilepsy and Cerebral Tumours.—The literature dealing with this subject is presented. Epileptic (epileptiform) fits are

found in about 25 to 30 per cent. of all cerebral tumours. The anatomical structure of the growth and its localization determine the incidence and type of the attacks. The epileptic manifestations must be regarded as expressions of local disturbances and are not due to the increased intracranial tension. Unanimity has not been reached in correlating the more detailed localization of tumours with the frequency of epileptic attacks, although the temporal lobes appear to be particularly prone to give rise to fits. The diagnosis from genuine epilepsy and the prognosis of patients suffering from cerebral tumour with epilepsy are briefly discussed. Benign tumours are more apt to give rise to epilepsy than are malignant. (J. S.)

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Circulation double d'un Angiome cerebral. (Double circulation in a cerebral angioma.) E. Moniz. 217.

*Gehirnschädigungen nach cerebraler Arteriographie mit Thorotrast. (Brain lesions after cerebral arteriography with Thorotrast.) G. Ekström and G. A. Lindgren. 227.

Die Vasomotorik der Hirndurchblutung. (The vasomotor mechanism of the cerebral circulation.) D. Schneider. 248.

Brain Lesions after Arteriography.—The brains of 35 patients who had died at varying periods after the performance of an arteriography were examined microscopically. In 60 per cent. of cases Thorotrast was found in some vessels and in six brains parenchymatous lesions could be correlated with the presence of Thorotrast in the form of small intravascular clots. The authors believe that central expansive lesions aid the retention of the Thorotrast and that a reduction in the thrombocyte count may be an important factor. No extravascular deposits of Thorotrast could be found. In the opinion of the authors some of the deaths were directly due to the arteriography. (J. S.)

BOOK REVIEWS

CONCEPTS AND PROBLEMS OF PSYCHOTHERAPY

L. E. Hinsie

(William Heinemann (Medical Books), Ltd., London. 1938. 15*s*.)

The author gives a clear outline of the principles of psychotherapy as practised by the schools of Freud, A. Meyer, Jung, and Adler. As is to be expected from the comparatively small volume, the work gives an introduction and stimulates the student to further studies ; the author does not pretend to present a complete textbook. Although he emphasizes that " it would not seem desirable at this time to express any final judgment with respect to any single school," his preference for the Freudian school of thought is obvious. He states that Adler's and Jung's " present position is in the periphery of psychiatric practice." Hence the chapter dealing with Adler and Jung occupies a tenth of the space occupied by those dealing with Freud and A. Meyer. In spite of this inequality the book may prove very useful for the student, and for those practitioners who need a primary introduction. In an appendix C. A. Landis gives a statistical analysis of therapeutic results obtained by psycho-analytical methods as published by various big hospitals ; he uses all the critical judgment necessary for such a purpose. The make-up of the book would improve considerably if the only picture (popular representation of various " streams " of the human psyche in the form of a landscape) were omitted.

THE HYPOTHALAMUS

W. E. Le Gros Clark, J. Beattie, G. Riddoch, and N. M. Dott

(Oliver and Boyd, Ltd., Edinburgh. 1938. 12*s*. 6*d*.)

In a book which is a record of four lectures given by four different individuals there is an excellent opportunity for the expression of a variety of opinions, and these are to be found herein. The first lecture, dealing with the structure of the hypothalamus, comprises a wide survey of this aspect of the study of the hypothalamus, and students will find much of interest. To collect in one lecture the knowledge of the function of this region of the brain is a task fraught with difficulty, and it is accordingly to be expected that some of the views expressed may meet with criticism. The clinician will turn to the next lecture with interest : again it is to be remembered that time allotted to one lecture permits only of a rapid review of the literature on clinical neurology. This lecture might have been made more interesting by the inclusion of " clinical " photographs such as appear in the lecture dealing with the surgical aspects. In the latter lecture the wealth of illustrations is unusual, the constant repetition of series of diagrams illustrative of operative technique becomes tiresome and appears unnecessary, while those pages in this section devoted to hypothalamic derangement are in the main a repetition of the lecture devoted to the clinical aspects. Should the book enter another edition, it is to be hoped that the display of unnecessary illustrations,

and especially those that are repetitive, will be avoided. More careful editing to exclude errors in references and a standard method of references would do much to alleviate the annoyance to the reader interested in this part of the nervous system who may wish to use the book.

A TEXTBOOK OF NEURORADIOLOGY

C. P. G. Wakeley and A. Orley

(Baillière, Tindall and Cox, London. 1938. 25*s*.)

It is some years since there has appeared any publication by English authors which has dealt at all comprehensively with the radiology of the central nervous system. This book is a much-needed addition to the literature on the subject. As the literature available in other languages is extraordinarily wide in extent, an admirable bibliography is appended to the book. It could be wished that the book itself had been somewhat expanded correspondingly. The reproductions of X-ray films, though good, might have been more numerous and used to a larger extent to illustrate the text. Too little technical detail is perhaps included for the radiologist, and insufficient illustration of the normal and its variations for the neurologist. The section on ventriculography is comprehensive and extremely clear. The earlier chapters might well have been treated in similar detail and further illustrated. This book will be found useful by neurologists.

THE PHARMACOLOGICAL SHOCK TREATMENT OF SCHIZOPHRENIA

M. Sakel

(Revised English Edition. Nervous and Mental Disease Publishing Co., New York and Washington. 1938. $2.75)

This book, originally written in German, now appears in English. Sakel's method of insulin treatment, his results, and his theoretical conceptions are so well known and have been the subject of so many recent discussions that it would be redundant to give an account of the contents of this monograph.

Foster-Kennedy in his preface considers Sakel's ideas underlying the treatment to be " the most important step made in psychiatric knowledge since we discovered the organic background of general paresis." Whether this is true or not only the future can tell. Nobody can deny, however, that the introduction of insulin treatment has opened new avenues of biochemical research in psychiatry of a most promising nature.

EXPERIMENTAL STUDIES OF COLOUR AND NON-COLOUR ATTITUDE IN SCHOOL CHILDREN AND ADULTS. Especially with Regard to its Condition in Different Types according to the Individual Psychology of Sjöbring and the Anthropometric Index of Strömgren

B. J. Lindberg

(Acta Psychiatrica et Neurologica, Supplementum XVI. Copenhagen. 1938.)

The author designed two tests for denoting a person's tendency to direct his attention primarily to the coloured or non-coloured elements of drawings. He

examined over 2,000 school children, over 200 patients of a surgical department of a general hospital, and over 400 psychiatric patients. Age, sex, intelligence, " liveliness " of the normals showed interesting correlations to the " attitude." In the psychiatric material, Lindberg confirmed the grouping of personalities according to the diagnostic system of his teacher, H. Sjöbring, by the results of his testing. Similarly, relations to certain bodily types were established.

PSYCHISCHE INSUFFIZIENZZUSTÄNDE BEI OLIGOPHRENIEN LEICHTEREN GRADES. EINE PERSÖNLICHKEITSANALYTISCHE UNTERSUCHUNG

E. Goldkuhl

(Acta Psychiatrica, Supplementum XV. Copenhagen. 1938.)

This monograph contains (1) a clinical description of psychoses in high-grade defectives, based upon 220 observations in the Psychiatric Clinic in Lund as well as on the literature of the subject, and (2) a psychological analysis of the patients' personalities intended to furnish a natural classification of the cases. The description both of the psychoses and of the character of the defectives is careful and detailed, and gives a very good picture of the variety of the personalities, a point which has been somewhat neglected until lately. For the purpose of classification the author uses Sjöbring's " fundamental factors of personality " ; the reader will find the analyses excellent once he has grown used to Sjöbring's peculiar terminology and understands that " sub-capacity " = mental defect, " sub-validity " = asthenic, " sub-solidity " = hysterical, and " sub-stability " = manic-depressive constitution respectively.

THE CLINICAL EXAMINATION OF THE NERVOUS SYSTEM

G. H. Monrad-Krohn

(Seventh Edition. H. K. Lewis & Co., London. 1938. 8*s.* 6*d.*)

We welcome the seventh edition of this well-known and deservedly popular handbook. It has much increased in size since the early editions, and now contains a short chapter on ventriculography and encephalography, accompanied by numerous and beautiful reproductions of normal and abnormal skiagrams. We would prefer the student to have the smaller edition, omitting such highly technical procedures, fearing that he may be unwilling to read so much and be unable to carry the present volume in his pocket. The cost has been kept remarkably low, especially considering the number of photographic plates and their general excellence throughout the book.

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